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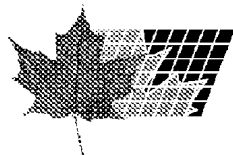
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(54) **COMPOSES DE PYRIMIDINE THIOALKYL ALPHA SUBSTITUES**

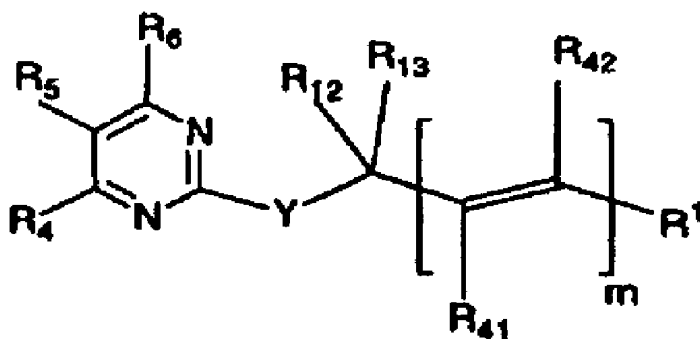
(54) **THIOALKYL ALPHA SUBSTITUTED PYRIMIDINE COMPOUNDS**

(57)

The subject invention relates to pyrimidine-thioalkyl and alkylether compounds of Formula (I) and pyrimidine-thiolalkyl and alkylethers of Formula (I), where R⁴ is selected from the group consisting of -H or -NR¹⁵R¹⁶ where R¹⁵ is -H and R¹⁶ is -H, C¹-C⁶ alkyl, -NH₂ or R¹⁵ and R¹⁶ taken together with the -N form 1- pyrrolidino, 1-morpholino or 1-piperidino; and R⁶ is -S-C¹-6 alkyl (preferably -SCH₃). The compounds of Formula (I) are useful in the treatment of individuals who are HIV positive.



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(54) **COMPOSES DE PYRIMIDINE THIOALKYL ALPHA
SUBSTITUES**
(54) **THIOALKYL ALPHA SUBSTITUTED PYRIMIDINE
COMPOUNDS**



(I)

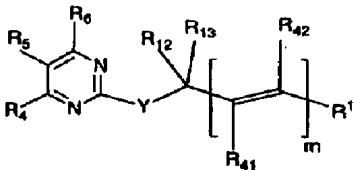
(57) L'invention concerne des composés à base de pyrimidinethioalkyl ou d'alkyléther qui correspondent à la formule suivante: (I) ainsi que pyrimidine thioalkyl et des alkyléthers qui correspondent à la formule (I), dans laquelle R₄ est sélectionné dans un groupe constitué de -H ou de -NR₁₅R₁₆ dans lequel R₁₅ est H et R₁₆ est -H, alkyle C₁-C₆, -NH₂ ou R₁₅ et R₁₆ pris avec 1-pyrrolidino, 1-morpholino ou 1-pipéridino de forme -N; et R₆ est -S-C₁₋₆ alkyl (de préférence -SCH₃); les composés de la formule (I) sont utiles dans le traitement des personnes VIH séropositives.

(57) The subject invention relates to pyrimidine-thioalkyl and alkylether compounds of Formula (I) and pyrimidine-thiolalkyl and alkylethers of Formula (I), where R₄ is selected from the group consisting of -H or -NR₁₅R₁₆ where R₁₅ is -H and R₁₆ is -H, C₁-C₆ alkyl, -NH₂ or R₁₅ and R₁₆ taken together with the -N form 1-pyrrolidino, 1-morpholino or 1-piperidino; and R₆ is -S-C₁₋₆ alkyl (preferably -SCH₃). The compounds of the formula (I) are useful in the treatment of individuals who are HIV positive.



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(21) International Application Number: PCT/US98/18507 (22) International Filing Date: 21 September 1998 (21.09.98) (30) Priority Data: 60/059,656 25 September 1997 (25.09.97) US (71) Applicant (for all designated States except US): PHARMACIA & UPJOHN COMPANY [US/US]; 301 Henrietta Street, Kalamazoo, MI 49001 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): MORRIS, Joel [US/US]; 3001 Applelane, Kalamazoo, MI 49008 (US). WISHKA, Donn, G. [US/US]; 1431 Northampton Road, Kalamazoo, MI 49006 (US). ADAMS, Wade, J. [US/US]; 744 Garland Avenue, Kalamazoo, MI 49008 (US). FRIIS, Janice, M. [US/US]; 8749 South 2nd Street, Mattawan, MI 49071 (US). (74) Agent: JAMESON, William, G.; Pharmacia & Upjohn Company, Intellectual Property Legal Services, 301 Henrietta Street, Kalamazoo, MI 49001 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>
(54) Title: THIOALKYL ALPHA SUBSTITUTED PYRIMIDINE COMPOUNDS <div style="text-align: center;">  <p>(I)</p> </div> (57) Abstract <p>The subject invention relates to pyrimidine-thioalkyl and alkylether compounds of Formula (I) and pyrimidine-thiolkyl and alkylethers of Formula (I), where R₄ is selected from the group consisting of -H or -NR₁₅R₁₆ where R₁₅ is -H and R₁₆ is -H, C₁-C₆ alkyl, -NH₂ or R₁₅ and R₁₆ taken together with the -N form 1-pyrrolidino, 1-morpholino or 1-piperidino; and R₆ is -S-C₁₋₆ alkyl (preferably -SCH₃). The compounds of Formula (I) are useful in the treatment of individuals who are HIV positive.</p>		

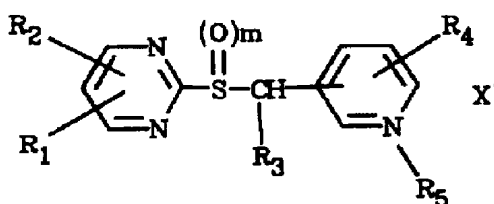
THIOALKYL ALPHA SUBSTITUTED PYRIMIDINE COMPOUNDS

BACKGROUND OF THE INVENTION1. Field of Invention

The 6-thioalkyl pyrimidine-2-thioalkyl and alkylether derivatives of Formula I are useful in the treatment of individuals who are HIV positive, whether or not they show AIDS symptoms at the present time. The 6-thioalkyl pyrimidine-2-thioalkyl and alkylether derivatives of Formula I are useful in the preparation of the pyrimidine-thioalkyl and alkylether derivatives of Formula I.

2. Description of the Related Art

U.S. Patent 5,025,016 (and EP 124 630) pyrimidine-thioalkyl pyridine derivatives corresponding to the general formula



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in which R_1 to R_4 , independently of one another, represent hydrogen, lower alkyl, halogen, amino or hydroxy groups, R_5 represents a free electron pair or a lower alkyl group, a halogen atom, m has the value 0 or 1, the pyrimidine-thioalkyl group being bonded in the 2-, 3- or 4-position of the pyridine ring, and to therapeutically compatible acid addition salts thereof. The compounds allegedly exhibit surprisingly improved bronchosecretolytic and myucolytic activity as well as having been found to show antiphlogistic activity.

J. Med Chem. 1987, 30, 547-551 describes various 2-[(pyridinylmethyl)thio]-pyrimidine derivatives and the influence thereof on bronchosecretolytic properties in the phenol red screening model of the mouse in comparison to the known drug ambroxol.

EP 477 778 (Derwent 92-106190/14) describes various benzene, pyridine and pyrimidine derivatives as ACAT enzyme inhibitors, for treating arteriosclerosis, and cerebrovascular disease.

J. Org. Chem, 1954, 19, 1793-1801 describes pyrimidine derivatives, including 2-benzylmercapto-4-amino-6-pyrimidinol, 2-benzylmercapto-4-amino-6-chloropyrimidine, 2-benzylmercapto-4-amino-6-diethylaminopyrimidine as well as analogs of 6-dimethylaminopurine.

British Patent 744,867 (CA 51:2063i) describes various 2-R'-S-6-RR'N-substituted 4-aminopyrimidines.

An estimated one to one and one-half million people in the United States are infected with a human retrovirus, the human immunodeficiency virus type I (HIV-1) which is the etiological agent of acquired immunodeficiency syndrome, AIDS, see Science, 661-662 (1986). Of those infected, an estimated two hundred and fifty thousand people will develop AIDS in the next five years, see Science, 1352-1357 (1985). On March 20, 1987, the FDA approved the use of the compound, AZT (zidovudine), to treat AIDS patients with a recent initial episode of pneumocystis carinii pneumonia, AIDS patients with conditions other than pneumocystis carinii pneumonia or patients infected with the virus with an absolute CD4 lymphocyte count of less than 200/mm³ in the peripheral blood. AZT is a known inhibitor of viral reverse transcriptase, an enzyme necessary for human immunodeficiency virus replication.

U.S. Patent 4,724,232 claims a method of treating humans having acquired immunodeficiency syndrome utilizing 3'-azido-3'-deoxy-thymidine (azidothymidine, AZT).

It is known in the art that certain antibiotics and polyanionic dyes inhibit retrovirus reverse transcriptase.

Many publications have reported the ability of various sulfated compounds to inhibit virus replication, including HIV.

Nature 343, 470 (1990) and Science 250, 1411 (1990) disclose potent benzodiazepin type reverse transcriptase inhibitors. The compounds of the present invention are not benzodiazepin type compounds.

J. Org. Chem. 1962, 27, 181-185 describes various 2-benzylthio pyrimidine derivatives, including 4-chloro-5-methyl-2-[(phenylmethyl)thio]-pyrimidine, 4-chloro-5-methyl-2-[(2,4-dichloro-phenyl)methyl]thio]-pyrimidine, 4-chloro-5-methyl-2-[(2-chloro-phenyl)methyl]thio]-pyrimidine, and 4-chloro-5-methyl-2-[(4-chloro-phenyl)methyl]thio]-pyrimidine and their activity as antitumor compounds in screens against SA-180, CA 755, and L-1210 tumor systems.

J. Med. Chem. 1977, 20, 88-92 describes 2-alkoxy and 2-alkylthio-4-amino pyrimidines, including 2-[(phenylmethyl)thio]4-pyrimidinamine, 2-[(4-chlorophenyl)methyl]thio]-4-pyrimidinamine, 2-[(3-pyridinylmethyl)thio]4-pyrimidinamine, and 2-(phenylmethoxy)-4-pyrimidinamine, and their activity as inhibitors of deoxycytidine kinase.

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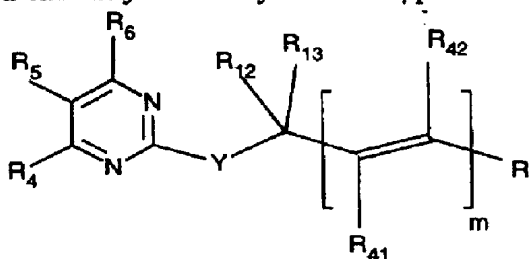
Collect. Czech. Chem. Comm. 1975, 40, 1078-1088 (CA 83:114326e) describes 5-(3-iodopropargyloxy)pyrimidines as effective fungistatics.

Synthesis 1981, 397-400 describes peroxy pyrimidines

J. Org. Chem. 1961, 26, 1884 describes the synthesis of aziridinyl pyrimidines
5 as analogs of methioprim.

J. Med. Chem. 1991, 34, 315-319 describes derivatives of thiouracil which have dihydroxyboryl group at the C-5 position. These compounds are useful for B neutron-capture therapy of malignant melanoma.

WO 96/35678 (published 14 November 1996) discloses various alpha-
10 substituted pyrimidine-2-thioalkyl and alkylether compounds of Formula A



wherein

R_4 is selected from the group consisting of -H, -OH, halo or $-NR_{15}R_{16}$ where R_{15} is -H and R_{16} is -H, C_1 - C_6 alkyl, $-NH_2$ or R_{15} and R_{16} taken together with the
20 -N form 1-pyrrolidino, 4-morpholino or 1-piperidino;

R_5 is selected from the group consisting of -H, $-C_2H_4OH$, $-C_2H_4-O-TBDMS$, halo, $-C_3$ - C_6 cycloalkyl, C_1 - C_3 alkoxy, $-CH_2CH_2Cl$ or C_1 - C_4 alkyl, with the proviso that R_5 is not isobutyl;

or R_4 and R_5 are taken together to form a five or six-membered saturated or
25 unsaturated ring which together with the pyrimidine ring form the group consisting of 7H-pyrrolo[2,3-d]pyrimidine, 5,6-dihydro-7H-pyrrolo[2,3-d]pyrimidine, furo[2,3-d]pyrimidine, 5,6-dihydro-furo[2,3-d]pyrimidine, thieno[2,3-d]pyrimidine, 5,6-dihydro-thieno[2,3-d]pyrimidine, 1H-pyrazolo[3,4-d]pyrimidine, 1H-purine, pyrimido[4,5-d]pyrimidine, pteridine, pyrido[2,3-d]pyrimidine, or quinazoline, where the
30 unsaturated ring may be optionally substituted with 1, 2 or 3, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, -OH, $-CH_2OH$, or $-(CH_2)_n-N(R_{31})(R_{32})$, $-C_3$ - C_8 cycloalkyl, $-CF_3$, -halo, $-CO_2(R_{31})$, $-CON(R_{31})(R_{32})$, $-CO(R_{31})$, $-(CH_2)_nN(R_{31})(CO(R_{33}))$, $-(CH_2)_nN(R_{31})(SO_2(R_{33}))$, and the saturated ring may be optionally substituted with 1, 2 or 3, $-C_1$ - C_6 alkyl, $-C_1$ - C_6 alkoxy, -OH, $-CH_2OH$, or $-(CH_2)_n-N(R_{31})(R_{32})$ or one oxo ($=O$);
35 and

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R_6 is selected from the group consisting of -H, -OH, halo (preferably -Cl), -CN, -CF₃, -CO₂(R₆₁), -C(O)R₆₁ or -C(O)N(R₆₁)(R₆₂) where R₆₁ and R₆₂ are the same or different and are selected from

-H,

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C₁-C₆ alkyl,

phenyl optionally substituted with 1, 2, or 3 -halo, C₁-C₆ alkyl, C₁-C₆ alkoxy, -CF₃, -OH, -CN,

or where R₆₁ and R₆₂ taken together with the attached nitrogen to form a ring selected from -pyrrolidinyl, -piperidinyl, -4-morpholinyl, -4-thiomorpholinyl,

10 -4-piperazinyl, or -4-(C₁-C₆ alkyl)piperazinyl;

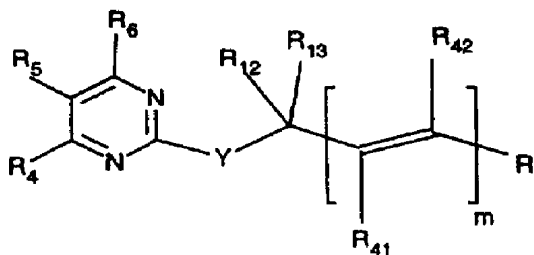
with the overall proviso that R₄ and R₆ are not both -H; and with the further proviso that and R₁₂ and R₁₃ are not both -H except when R₆ is selected from -CN, -CF₃, -CO₂(R₆₁), -C(O)R₆₁ or -C(O)N(R₆₁)(R₆₂), or R₁ is selected from -CO₂R₅₃ or -C(O)N(R₅₄)(R₅₅);

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SUMMARY OF INVENTION

Disclosed are 6-thioalkyl pyrimidine-2-thioalkyl and alkylether compounds of Formula I

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and therapeutically/pharmaceutically compatible acid addition salts thereof.

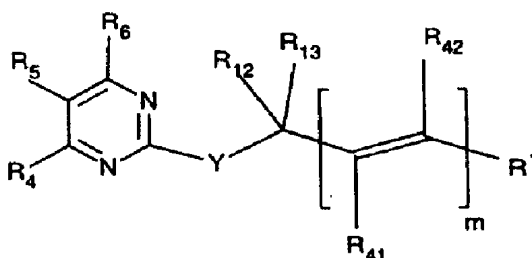
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The compounds corresponding to Formula I may exist in various tautomeric formulas, and are included within the scope of Formula I.

DETAILED DESCRIPTION OF THE INVENTION

Disclosed are 6-thioalkyl pyrimidine-2-thioalkyl and alkylether compounds of Formula I

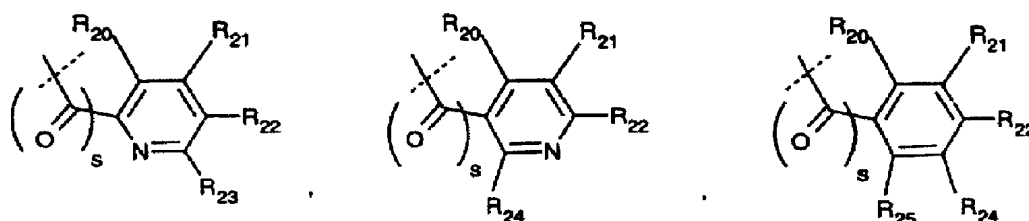
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where m is 0 or 1;

R^1 is selected from the group consisting of $-C\equiv CH$, $-CO_2R_{53}$, $-CONR_{54}R_{55}$,

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where s is 0 or 1 (preferably 0) and R_{20} , R_{21} , R_{22} , R_{23} , R_{24} , and R_{25} are the same or different and are selected from $-H$, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkoxy, C_1-C_6 alkylthio, $-C_3-C_8$ cycloalkyl, $-CF_3$, $-NO_2$, $-halo$, $-OH$, $-CN$, phenyl, phenylthio, $-styryl$, $-CO_2(R_{31})$, $-CON(R_{31})$ (R_{32}), $-CO(R_{31})$, $-(CH_2)_n-N(R_{31})(R_{32})$, $-C(OH)(R_{31})(R_{33})$, $-(CH_2)_n-N(R_{31})(CO(R_{33}))$, $-(CH_2)_n-N(R_{31})(SO_2(R_{33}))$, or where R_{20} and R_{21} , or R_{21} and R_{22} , or R_{22} and R_{23} are taken together to form a five or six-membered saturated or unsaturated ring containing 0 or 1

25

oxygen, nitrogen or sulfur, where the unsaturated ring may be optionally substituted with 1, 2 or 3, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-OH$, $-CH_2OH$, $-(CH_2)_n-N(R_{31})(R_{32})$, $-C_3-C_8$ cycloalkyl, $-CF_3$, $-halo$, $CO_2(R_{31})$, $-CON(R_{31})(R_{32})$, $-CO(R_{31})$, $-(CH_2)_n-N(R_{31})(CO(R_{33}))$, $-(CH_2)_n-N(R_{31})(SO_2(R_{33}))$, $-CN$, $-CH_2CF_3$ or $-CH(CF_3)_2$, or phenyl, and the saturated ring may be optionally substituted with 1, 2 or 3, $-C_1-C_6$ alkyl, $-C_1-C_6$ alkoxy, $-OH$, $-CH_2OH$ or $-(CH_2)_n-N(R_{31})(R_{32})$ or one oxo ($=O$);

30

where n is 0-3 and R_{31} , R_{32} , and R_{33} are the same or different and are selected from

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$-H$,
 C_1-C_6 alkyl,

phenyl optionally substituted with 1, 2, or 3 -halo, C₁-C₆ alkyl,

C₁-C₆ alkoxy, -CF₃, -OH or -CN,

or where R₃₁ and R₃₂ taken together with the attached nitrogen to form a ring selected from -pyrrolidinyl, -piperidinyl, -4-morpholinyl, -4-thiomorpholinyl, -4-

5 piperazinyl, -4-(1-C₁-C₆alkyl)piperazinyl,

or a member selected from the group consisting of:

1-cyclohexenyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 2-imidazolyl,

4-imidazolyl, 2-benzothiazolyl, 2-benzoxazolyl, 2-benzimidazolyl, 2-oxazolyl,

4-oxazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 5-methyl-3-isoxazolyl, 5-

10 phenyl-3-isoxazolyl, 4-thiazolyl, 3-methyl-2-pyrazinyl, 5-methyl-2-pyrazinyl, 6-

methyl-2-pyrazinyl, 5-chloro-2-thienyl, 3-furyl, benzofuran-2-yl, benzothien-2-

yl, 2H-1-benzopyran-3-yl, 2,3-dihydrobenzopyran-5-yl, 1-methylimidazol-2-yl,

quinoxalin-2-yl, piperon-5-yl, 4,7-dichlorobenzoxazol-2-yl, 4,6-dimethyl-

pyrimidin-2-yl, 4-methylpyrimidin-2-yl, 2,4-dimethylpyrimidin-6-yl, 2-

15 methylpyrimidin-4-yl, 4-methylpyrimidin-6-yl, 6-chloropiperon-5-yl, 5-

chloroimidazo[1,2-a]pyridin-2-yl, 1-H-inden-3-yl, 1-H-2-methyl-inden-2-yl, 3,4-

dihydronaphth-1-yl, S-4-isopropenylcyclohexen-1-yl or 4-dihydronaphth-2-yl;

where R₅₃ is selected from the group consisting of -H, C₁-C₆alkyl, C₃-

C₆cycloalkyl, phenyl (optionally substituted with 1, 2, or 3 -halo,

20 C₁-C₆ alkyl, C₁-C₆ alkoxy, -CF₃, -OH, -CN), or a five or six-membered unsaturated ring containing 0 or 1 oxygen, nitrogen or sulfur, where the unsaturated ring may be optionally substituted with -H, C₁-C₆ alkyl,

C₁-C₆ alkoxy, -OH, -CH₂OH, or -(CH₂)_n-N(R₃₁)(R₃₂);

where R₅₄ and R₅₅ being the same or different are selected from -H,

25 C₁-C₆ alkyl, allyl, or phenyl (optionally substituted with 1, 2, or 3

-halo, C₁-C₆ alkyl, C₁-C₆ alkoxy or -CF₃), or taken together with the

attached nitrogen to form a ring selected from -pyrrolidinyl,

-piperidinyl, -4-morpholinyl, -4-thiomorpholinyl, -4-piperazinyl,

-4-(1-C₁-C₆alkyl)piperazinyl;

30 R₄₁ and R₄₂, being the same or different, are selected from the group consisting of -H and C₁-C₄ alkyl;

R₁₂ is selected from the group consisting of -H, C₁-C₆ alkyl,

-C₃-C₆ cycloalkyl, -CN, -C(O)NH₂, -C(O)N(C₁-C₆alkyl)(C₁-C₆alkyl), -CO₂H,

-CO₂(C₁-C₆alkyl), -CH₂OH, -CH₂NH₂ or -CF₃;

35 R₁₃ is selected from the group consisting of -H, C₁-C₆ alkyl or -CF₃;

Y is selected from -S-, -S(O)-, -S(O)₂, or -O-;

R_4 is selected from the group consisting of -H, -OH, halo or $-NR_{15}R_{16}$ where R_{15} is -H and R_{16} is -H, C_1-C_6 alkyl, $-NH_2$ or R_{15} and R_{16} taken together with the -N form 1-pyrrolidino, 4-morpholino or 1-piperidino;

R_5 is selected from the group consisting of -H, $-C_2H_4OH$, $-C_2H_4-O-TBDMS$,
 5 halo, $-C_3-C_6$ cycloalkyl, C_1-C_3 alkoxy,
 $-CH_2CH_2Cl$ or C_1-C_4 alkyl, with the proviso that R_5 is not isobutyl;

or R_4 and R_5 are taken together to form a five or six-membered saturated or unsaturated ring which together with the pyrimidine ring form the group consisting of 7H-pyrrolo[2,3-d]pyrimidine, 5,6-dihydro-7H-pyrrolo[2,3-d]pyrimidine, furo[2,3-
 10 d]pyrimidine, 5,6-dihydro-furo[2,3-d]pyrimidine, thieno[2,3-d]pyrimidine, 5,6-dihydro-thieno[2,3-d]pyrimidine, 1H-pyrazolo[3,4-d]pyrimidine, 1H-purine, pyrimido[4,5-d]pyrimidine, pteridine, pyrido[2,3-d]pyrimidine, or quinazoline, where the unsaturated ring may be optionally substituted with 1, 2 or 3, C_1-C_6 alkyl, C_1-C_6 alkoxy, -OH, $-CH_2OH$, or $-(CH_2)_n-N(R_{31})(R_{32})$, $-C_3-C_8$ cycloalkyl, $-CF_3$, -halo, -
 15 $CO_2(R_{31})$, $-CON(R_{31})(R_{32})$, $-CO(R_{31})$, $-(CH_2)_nN(R_{31})(CO(R_{33}))$, $-(CH_2)_nN(R_{31})(SO_2(R_{33}))$, and the saturated ring may be optionally substituted with 1, 2 or 3, $-C_1-C_6$ alkyl, $-C_1-C_6$ alkoxy, -OH, $-CH_2OH$, or $-(CH_2)_n-N(R_{31})(R_{32})$ or one oxo (=O); and

R_6 is $-S-C_{1-6}$ alkyl (preferably $-S-CH_3$);

pharmaceutically acceptable salts, hydrates, N-oxides and solvates thereof.

20 An embodiment of the present invention are compounds of Formula I where R_{12} and R_{13} are not both -H.

An embodiment of the present invention are 6-thioalkyl pyrimidine-2-thioalkyl and alkyl ether anti-AIDS compounds of Formula I where

R_4 is selected from the group consisting of -H or $-NR_{15}R_{16}$ where R_{15} is -H
 25 and R_{16} is -H, C_1-C_6 alkyl, $-NH_2$ or R_{15} and R_{16} taken together with the -N form 1-pyrrolidino, 4-morpholino or 1-piperidino; and

R_6 is $-S-C_{1-6}$ alkyl (preferably $-S-CH_3$).

The compounds of Formula I can be prepared in accordance with the procedures disclosed in WO 96/35678 as well as US Patent Application Serial No.
 30 08/436,708; filed 8 May 1995, both of which are incorporated herein by reference.

An embodiment of the present invention are compounds of Formula I where Y is -O-.

A preferred embodiment of the present invention are compounds of Formula I where s is 0 and Y is selected from the group consisting of -S-, $-S(O)-$ or $-S(O)_2$;
 35 more preferably Y is -S-.

A preferred embodiment of the present invention are compounds of Formula I

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where s is 0 and Y is selected from the group consisting of -S-, -S(O)- or -S(O)₂ (more preferably Y is -S-); and with the proviso that R₁₂ and R₁₃ are not both -H.

R₄ is preferably -NH₂.

m is preferably 0.

5 R₆ is preferably -S-CH₃.

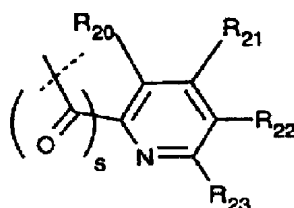
R₄₁ and R₄₂ are preferably -H.

R₁₂ is preferably -CH₃.

R₁₃ is preferably -H.

R¹ is preferably selected from

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15

more preferably a member selected from the group consisting of:

3-isoquinoliny, 1-isoquinoliny, 2-quinoliny, 3-quinoliny, 3-(5,6,7,8-tetrahydro)-
isoquinoliny, 1-(5,6,7,8-tetrahydro)-isoquinoliny, 2-(5,6,7,8-tetrahydro)-quinoliny, 3-
20 (5,6,7,8-tetrahydro)-quinoliny, 3-(5,6-dihydro)-2H-2-pyrindiny, 1-(5,6-dihydro)-2H-2-
pyrindiny, 2-(5,6-dihydro)-1H-1-pyrindiny, 3-(5,6-dihydro)-1H-1-pyrindiny, 5-
furo[2,3-c]pyridiny, 6-furo[3,2-c]pyridiny, 4-furo[3,2-c]pyridiny, 7-furo[2,3-
c]pyridiny, 6-furo[2,3-b]pyridiny, 5-furo[3,2-b]pyridiny, 5-(2,3-dihydro)-furo[2,3-
c]pyridiny, 6-(2,3-dihydro)-furo[3,2-c]pyridiny, 4-(2,3-dihydro)-furo[3,2-c]pyridiny,
25 7-

(2,3-dihydro)-furo[2,3-c]pyridiny, 6-(2,3-dihydro)-furo[2,3-b]pyridiny, 5-(2,3-dihydro)-
furo[3,2-b]pyridiny, 6-(1,3-dihydro)-furo[3,4-c]pyridiny, 4-(1,3-dihydro)-furo[3,4-
c]pyridiny, 2-(5,7-dihydro)-furo[3,4-b]pyridiny, 6-(3,4-dihydro)-2H-pyrano[2,3-
c]pyridiny, 6-(3,4-dihydro)-1H-pyrano[3,4-c]pyridiny, 7-(3,4-dihydro)-1H-pyrano[4,3-
30 c]pyridiny, 7-(3,4-dihydro)-2H-pyrano[3,2-c]pyridiny, 5-(3,4-dihydro)-2H-pyrano[3,2-
c]pyridiny, 5-(3,4-dihydro)-1H-pyrano[4,3-c]pyridiny, 8-(3,4-dihydro)-1H-pyrano[3,4-
c]pyridiny, 8-(3,4-dihydro)-2H-pyrano[2,3-c]pyridiny, 7-(3,4-dihydro)-2H-pyrano[2,3-
b]pyridiny, 2-(5,6-dihydro)-1H-pyrano[3,4-b]pyridiny, 2-(5,6-dihydro)-2H-pyrano[4,3-
b]pyridiny, 6-(3,4-dihydro)-2H-pyrano[3,2-b]pyridiny, 5-1H-pyrrolo[2,3-c]pyridiny,
35 6-1H-pyrrolo[3,2-c]pyridiny, 4-1H-pyrrolo[3,2-c]pyridiny, 7-1H-pyrrolo[2,3-
c]pyridiny, 6-1H-pyrrolo[2,3-b]pyridiny, 5-1H-pyrrolo[3,2-b]pyridiny, 5-(2,3-

- dihydro)-1H-pyrrolo[2,3-c]pyridinyl, 6-(2,3-dihydro)-1H-pyrrolo[3,2-c]pyridinyl, 4-(2,3-dihydro)-1H-pyrrolo[3,2-c]pyridinyl, 7-(2,3-dihydro)-1H-pyrrolo[2,3-c]pyridinyl, 6-(2,3-dihydro)-1H-pyrrolo[2,3-b]pyridinyl, 5-(2,3-dihydro)-1H-pyrrolo[3,2-b]pyridinyl, 6-(1,3-dihydro)-1H-pyrrolo[3,4-c]pyridinyl, 4-(1,3-dihydro)-1H-pyrrolo[3,4-c]pyridinyl, 2-
- 5 (5,7-dihydro)-1H-pyrrolo[3,4-b]pyridinyl, 6-1,7-naphthyridinyl, 6-2,7-naphthyridinyl, 7-2,6-naphthyridinyl, 7-1,6-naphthyridinyl, 5-1,6-naphthyridinyl, 5-2,6-naphthyridinyl, 8-2,7-naphthyridinyl, 8-1,7-naphthyridinyl, 7-1,8-naphthyridinyl, 2-1,7-naphthyridinyl, 2-1,6-naphthyridinyl, 6-1,5-naphthyridinyl, 6-(1,2,3,4-tetrahydro)-1,7-naphthyridinyl, 6-(1,2,3,4-tetrahydro)-2,7-naphthyridinyl, 7-(1,2,3,4-
- 10 tetrahydro)-2,6-naphthyridinyl, 7-(1,2,3,4-tetrahydro)-1,6-naphthyridinyl, 5-(1,2,3,4-tetrahydro)-1,6-naphthyridinyl, 5-(1,2,3,4-tetrahydro)-2,6-naphthyridinyl, 8-(1,2,3,4-tetrahydro)-2,7-naphthyridinyl, 8-(1,2,3,4-tetrahydro)-1,7-naphthyridinyl, 7-(1,2,3,4-tetrahydro)-1,8-naphthyridinyl, 2-(5,6,7,8-tetrahydro)-1,7-naphthyridinyl, 2-(5,6,7,8-tetrahydro)-1,6-naphthyridinyl, 6-(1,2,3,4-tetrahydro)-1,5-naphthyridinyl, 1-naphthyl,
- 15 2-naphthyl, 5-(1,2,3,4-tetrahydro)-naphthyl, 6-(1,2,3,4-tetrahydro)-naphthyl, 4-(2,3-dihydro)-1H-indenyl, 5-(2,3-dihydro)-1H-indenyl, 5-benzofuranyl, 4-benzofuranyl, 6-benzofuranyl, 7-benzofuranyl, 5-(2,3-dihydro)-benzofuranyl, 4-(2,3-dihydro)-benzofuranyl, 6-(2,3-dihydro)-benzofuranyl, 7-(2,3-dihydro)-benzofuranyl, 4-(1,3-dihydro)-isobenzofuran, 5-(1,3-dihydro)-isobenzofuran, 4-1H-indolyl, 5-1H-indolyl, 6-
- 20 1H-indolyl, 7-1H-indolyl, 4-(2,3-dihydro)-1H-indolyl, 5-(2,3-dihydro)-1H-indolyl, 6-(2,3-dihydro)-1H-indolyl, 7-(2,3-dihydro)-1H-indolyl, 4-(1,3-dihydro)-1H-isindolyl, 5-(1,3-dihydro)-1H-isindolyl, 5-(3,4-dihydro)-1H-2-benzopyranyl, 6-(3,4-dihydro)-1H-2-benzopyranyl, 7-(3,4-dihydro)-1H-2-benzopyranyl, 8-(3,4-dihydro)-1H-2-benzopyranyl, 5-(3,4-dihydro)-2H-1-benzopyranyl, 6-(3,4-dihydro)-2H-1-
- 25 benzopyranyl, 7-(3,4-dihydro)-2H-1-benzopyranyl, 8-(3,4-dihydro)-2H-1-benzopyranyl, 5-(1,2,3,4-tetrahydro)-isoquinolinyl, 6-(1,2,3,4-tetrahydro)-isoquinolinyl, 7-(1,2,3,4-tetrahydro)-isoquinolinyl, 8-(1,2,3,4-tetrahydro)-isoquinolinyl, 5-(1,2,3,4-tetrahydro)-quinolinyl, 6-(1,2,3,4-tetrahydro)-quinolinyl, 7-(1,2,3,4-tetrahydro)-quinolinyl, 8-(1,2,3,4-tetrahydro)-quinolinyl, 5-thieno[2,3-c]pyridinyl, 6-thieno[3,2-c]pyridinyl, 4-
- 30 thieno[3,2-c]pyridinyl, 7-thieno[2,3-c]pyridinyl, 6-thieno[2,3-b]pyridinyl, 5-thieno[3,2-b]pyridinyl, 5-(2,3-dihydro)-thieno[2,3-c]pyridinyl, 6-(2,3-dihydro)-thieno[3,2-c]pyridinyl, 4-(2,3-dihydro)-thieno[3,2-c]pyridinyl, 7-(2,3-dihydro)-thieno[2,3-c]pyridinyl, 6-(2,3-dihydro)-thieno[2,3-b]pyridinyl, 5-(2,3-dihydro)-thieno[3,2-b]pyridinyl, 6-(1,3-dihydro)-thieno[3,4-c]pyridinyl, 4-(1,3-dihydro)-thieno[3,4-
- 35 c]pyridinyl, 2-(5,7-dihydro)-thieno[3,4-b]pyridinyl, 6-(3,4-dihydro)-2H-thiopyrano[2,3-c]pyridinyl, 6-(3,4-dihydro)-1H-thiopyrano[3,4-c]pyridinyl, 7-(3,4-dihydro)-1H-

- thiopyrano[4,3-c]pyridinyl, 7-(3,4-dihydro)-2H-thiopyrano[3,2-c]pyridinyl, 5-(3,4-dihydro)-2H-thiopyrano[3,2-c]pyridinyl, 5-(3,4-dihydro)-1H-thiopyrano[4,3-c]pyridinyl, 8-(3,4-dihydro)-1H-thiopyrano[3,4-c]pyridinyl, 8-(3,4-dihydro)-2H-thiopyrano[2,3-c]pyridinyl, 7-(3,4-dihydro)-2H-thiopyrano[2,3-b]pyridinyl, 2-(5,6-dihydro)-1H-
- 5 thiopyrano[3,4-b]pyridinyl, 2-(5,6-dihydro)-2H-thiopyrano[4,3-b]pyridinyl, 6-(3,4-dihydro)-2H-thiopyrano[3,2-b]pyridinyl, 5-benzo[b]thiophenyl, 4-benzo[b]thiophenyl, 6-benzo[b]thiophenyl, 7-benzo[b]thiophenyl, 5-(2,3-dihydro)-benzo[b]thiophenyl, 4-(2,3-dihydro)-benzo[b]thiophenyl, 6-(2,3-dihydro)-benzo[b]thiophenyl, 7-(2,3-dihydro)-benzo[b]thiophenyl, 4-(1,3-dihydro)-benzo[c]thiophenyl, 5-(1,3-dihydro)-
- 10 benzo[c]thiophenyl, 5-(3,4-dihydro)-1H-2-benzothiopyranyl, 6-(3,4-dihydro)-1H-2-benzothiopyranyl, 7-(3,4-dihydro)-1H-2-benzothiopyranyl, 8-(3,4-dihydro)-1H-2-benzothiopyranyl, 5-(3,4-dihydro)-2H-1-benzothiopyranyl, 6-(3,4-dihydro)-2H-1-benzothiopyranyl, 7-(3,4-dihydro)-2H-1-benzothiopyranyl, or 8-(3,4-dihydro)-2H-1-benzothiopyranyl; wherein such member is optionally substituted as described
- 15 above;
- most preferably a member selected from the group consisting of:
- 3-isoquinolinyl, 1-isoquinolinyl, 2-quinolinyl, 3-quinolinyl, 3-(5,6,7,8-tetrahydro)-isoquinolinyl, 1-(5,6,7,8-tetrahydro)-isoquinolinyl, 2-(5,6,7,8-tetrahydro)-quinolinyl, 3-(5,6,7,8-tetrahydro)-quinolinyl, 3-(5,6-dihydro)-2H-2-pyrindinyl, 1-(5,6-dihydro)-2H-2-
- 20 pyrindinyl, 2-(5,6-dihydro)-1H-1-pyrindinyl, 3-(5,6-dihydro)-1H-1-pyrindinyl, 5-furo[2,3-c]pyridinyl, 6-furo[3,2-c]pyridinyl, 4-furo[3,2-c]pyridinyl, 7-furo[2,3-c]pyridinyl, 6-furo[2,3-b]pyridinyl, 5-furo[3,2-b]pyridinyl, 5-(2,3-dihydro)-furo[2,3-c]pyridinyl, 6-(2,3-dihydro)-furo[3,2-c]pyridinyl, 4-(2,3-dihydro)-furo[3,2-c]pyridinyl, 7-(2,3-dihydro)-furo[2,3-c]pyridinyl, 6-(2,3-dihydro)-furo[2,3-b]pyridinyl, 5-(2,3-
- 25 dihydro)-furo[3,2-b]pyridinyl, 6-(1,3-dihydro)-furo[3,4-c]pyridinyl, 4-(1,3-dihydro)-furo[3,4-c]pyridinyl, 2-(5,7-dihydro)-furo[3,4-b]pyridinyl, 6-(3,4-dihydro)-2H-pyrano[2,3-c]pyridinyl, 6-(3,4-dihydro)-1H-pyrano[3,4-c]pyridinyl, 7-(3,4-dihydro)-1H-pyrano[4,3-c]pyridinyl, 7-(3,4-dihydro)-2H-pyrano[3,2-c]pyridinyl, 5-(3,4-dihydro)-2H-pyrano[3,2-c]pyridinyl, 5-(3,4-dihydro)-1H-pyrano[4,3-c]pyridinyl, 8-(3,4-dihydro)-1H-
- 30 pyrano[3,4-c]pyridinyl, 8-(3,4-dihydro)-2H-pyrano[2,3-c]pyridinyl, 7-(3,4-dihydro)-2H-pyrano[2,3-b]pyridinyl, 2-(5,6-dihydro)-1H-pyrano[3,4-b]pyridinyl, 2-(5,6-dihydro)-2H-pyrano[4,3-b]pyridinyl, or 6-(3,4-dihydro)-2H-pyrano[3,2-b]pyridinyl; wherein such member is optionally substituted as described above.

Illustrative R₁ members include:

- 35 phenyl optionally substituted with one, 2 or 3 C₁-C₄ alkyl, C₁-C₃ alkoxy, halo, C₁-C₃ alkylthio, trifluoromethyl, C₂-C₆ dialkylamino, or nitro; 2- or 3-pyridinyl

optionally substituted with C₁-C₆ alkyl, C₁-C₆ alkenyl, C₁-C₆ alkoxy, C₁-C₆ alkylthio, -C₃-C₈ cycloalkyl, -CF₃, -NO₂, -halo, -OH, -CN, phenyl, phenylthio, -styryl, -CO₂(R₃₁), -CON(R₃₁)(R₃₂), -CO(R₃₁), -(CH₂)_n-N(R₃₁)(R₃₂), -C(OH)(R₃₁)(R₃₃), -(CH₂)_n-N(R₃₁)(CO(R₃₃)), -(CH₂)_n-N(R₃₁)(SO₂(R₃₃)); naphthyl optionally substituted

5 with one or 2 C₁-C₄ alkyl, C₁-C₃ alkoxy, halo, trifluoromethyl, C₂-C₆ dialkylamino, C₁-C₃ alkylthio or nitro; -C≡CH; as well as 3-isoquinoliny, 1-isoquinoliny, 2-quinoliny, 3-quinoliny, 3-(5,6,7,8-tetrahydro)-isoquinoliny, 1-(5,6,7,8-tetrahydro)-isoquinoliny, 2-(5,6,7,8-tetrahydro)-quinoliny, 3-(5,6,7,8-tetrahydro)-quinoliny, 3-(5,6-dihydro)-2H-2-pyrindiny, 1-(5,6-dihydro)-2H-2-pyrindiny, 2-(5,6-dihydro)-1H-1-

10 pyrindiny, 3-(5,6-dihydro)-1H-1-pyrindiny, 5-furo[2,3-c]pyridiny, 6-furo[3,2-c]pyridiny, 4-furo[3,2-c]pyridiny, 7-furo[2,3-c]pyridiny, 6-furo[2,3-b]pyridiny, 5-furo[3,2-b]pyridiny, 5-(2,3-dihydro)-furo[2,3-c]pyridiny, 6-(2,3-dihydro)-furo[3,2-c]pyridiny, 4-(2,3-dihydro)-furo[3,2-c]pyridiny, 7-(2,3-dihydro)-furo[2,3-c]pyridiny, 6-(2,3-dihydro)-furo[2,3-b]pyridiny, 5-(2,3-dihydro)-furo[3,2-b]pyridiny, 6-(1,3-

15 dihydro)-furo[3,4-c]pyridiny, 4-(1,3-dihydro)-furo[3,4-c]pyridiny, 2-(5,7-dihydro)-furo[3,4-b]pyridiny, 6-(3,4-dihydro)-2H-pyrano[2,3-c]pyridiny, 6-(3,4-dihydro)-1H-pyrano[3,4-c]pyridiny, 7-(3,4-dihydro)-1H-pyrano[4,3-c]pyridiny, 7-(3,4-dihydro)-2H-pyrano[3,2-c]pyridiny, 5-(3,4-dihydro)-2H-pyrano[3,2-c]pyridiny, 5-(3,4-dihydro)-1H-pyrano[4,3-c]pyridiny, 8-(3,4-dihydro)-1H-pyrano[3,4-c]pyridiny, 8-(3,4-dihydro)-2H-

20 pyrano[2,3-c]pyridiny, 7-(3,4-dihydro)-2H-pyrano[2,3-b]pyridiny, 2-(5,6-dihydro)-1H-pyrano[3,4-b]pyridiny, 2-(5,6-dihydro)-2H-pyrano[4,3-b]pyridiny, 6-(3,4-dihydro)-2H-pyrano[3,2-b]pyridiny, 5-1H-pyrrolo[2,3-c]pyridiny, 6-1H-pyrrolo[3,2-c]pyridiny, 4-1H-pyrrolo[3,2-c]pyridiny, 7-1H-pyrrolo[2,3-c]pyridiny, 6-1H-pyrrolo[2,3-b]pyridiny, 5-1H-pyrrolo[3,2-b]pyridiny, 5-(2,3-dihydro)-1H-pyrrolo[2,3-c]pyridiny, 6-(2,3-

25 dihydro)-1H-pyrrolo[3,2-c]pyridiny, 4-(2,3-dihydro)-1H-pyrrolo[3,2-c]pyridiny, 7-(2,3-dihydro)-1H-pyrrolo[2,3-c]pyridiny, 6-(2,3-dihydro)-1H-pyrrolo[2,3-b]pyridiny, 5-(2,3-dihydro)-1H-pyrrolo[3,2-b]pyridiny, 6-(1,3-dihydro)-1H-pyrrolo[3,4-c]pyridiny, 4-(1,3-dihydro)-1H-pyrrolo[3,4-c]pyridiny, 2-(5,7-dihydro)-1H-pyrrolo[3,4-b]pyridiny, 6-1,7-

30 naphthyridiny, 6-2,7-naphthyridiny, 7-2,6-naphthyridiny, 7-1,6-naphthyridiny, 5-1,6-naphthyridiny, 5-2,6-naphthyridiny, 8-2,7-naphthyridiny, 8-1,7-naphthyridiny, 7-1,8-naphthyridiny, 2-1,7-naphthyridiny, 2-1,6-naphthyridiny, 6-1,5-naphthyridiny, 6-(1,2,3,4-tetrahydro)-1,7-naphthyridiny, 6-(1,2,3,4-tetrahydro)-2,7-naphthyridiny, 7-(1,2,3,4-tetrahydro)-2,6-naphthyridiny, 7-(1,2,3,4-tetrahydro)-1,6-naphthyridiny, 5-(1,2,3,4-tetrahydro)-1,6-naphthyridiny, 5-(1,2,3,4-tetrahydro)-2,6-

35 naphthyridiny, 8-(1,2,3,4-tetrahydro)-2,7-naphthyridiny, 8-(1,2,3,4-tetrahydro)-1,7-naphthyridiny, 7-(1,2,3,4-tetrahydro)-1,8-naphthyridiny, 2-(5,6,7,8-tetrahydro)-1,7-

- naphthyridinyl, 2-(5,6,7,8-tetrahydro)-1,6-naphthyridinyl, 6-(1,2,3,4-tetrahydro)-1,5-naphthyridinyl, 1-naphthyl, 2-naphthyl, 5-(1,2,3,4-tetrahydro)-naphthyl, 6-(1,2,3,4-tetrahydro)-naphthyl, 4-(2,3-dihydro)-1H-indenyl, 5-(2,3-dihydro)-1H-indenyl, 5-benzofuranyl, 4-benzofuranyl, 6-benzofuranyl, 7-benzofuranyl, 5-(2,3-dihydro)-
- 5 benzofuranyl, 4-(2,3-dihydro)-benzofuranyl, 6-(2,3-dihydro)-benzofuranyl, 7-(2,3-dihydro)-benzofuranyl, 4-(1,3-dihydro)-isobenzofuran, 5-(1,3-dihydro)-isobenzofuran, 4-1H-indolyl, 5-1H-indolyl, 6-1H-indolyl, 7-1H-indolyl, 4-(2,3-dihydro)-1H-indolyl, 5-(2,3-dihydro)-1H-indolyl, 6-(2,3-dihydro)-1H-indolyl, 7-(2,3-dihydro)-1H-indolyl, 4-(1,3-dihydro)-1H-isoindolyl, 5-(1,3-dihydro)-1H-isoindolyl, 5-(3,4-dihydro)-1H-2-
- 10 benzopyranyl, 6-(3,4-dihydro)-1H-2-benzopyranyl, 7-(3,4-dihydro)-1H-2-benzopyranyl, 8-(3,4-dihydro)-1H-2-benzopyranyl, 5-(3,4-dihydro)-2H-1-benzopyranyl, 6-(3,4-dihydro)-2H-1-benzopyranyl, 7-(3,4-dihydro)-2H-1-benzopyranyl, 8-(3,4-dihydro)-2H-1-benzopyranyl, 5-(1,2,3,4-tetrahydro)-isoquinolinyl, 6-(1,2,3,4-tetrahydro)-
- 15 isoquinolinyl, 7-(1,2,3,4-tetrahydro)-isoquinolinyl, 8-(1,2,3,4-tetrahydro)-isoquinolinyl, 5-(1,2,3,4-tetrahydro)-quinolinyl, 6-(1,2,3,4-tetrahydro)-quinolinyl, 7-(1,2,3,4-tetrahydro)-quinolinyl, 8-(1,2,3,4-tetrahydro)-quinolinyl, 5-thieno[2,3-c]pyridinyl, 6-thieno[3,2-c]pyridinyl, 4-thieno[3,2-c]pyridinyl, 7-thieno[2,3-c]pyridinyl, 6-thieno[2,3-b]pyridinyl, 5-thieno[3,2-b]pyridinyl, 5-(2,3-dihydro)-thieno[2,3-c]pyridinyl, 6-(2,3-dihydro)-thieno[3,2-c]pyridinyl, 4-(2,3-dihydro)-thieno[3,2-c]pyridinyl, 7-(2,3-dihydro)-
- 20 thieno[2,3-c]pyridinyl, 6-(2,3-dihydro)-thieno[2,3-b]pyridinyl, 5-(2,3-dihydro)-thieno[3,2-b]pyridinyl, 6-(1,3-dihydro)-thieno[3,4-c]pyridinyl, 4-(1,3-dihydro)-thieno[3,4-c]pyridinyl, 2-(5,7-dihydro)-thieno[3,4-b]pyridinyl, 6-(3,4-dihydro)-2H-thiopyrano[2,3-c]pyridinyl, 6-(3,4-dihydro)-1H-thiopyrano[3,4-c]pyridinyl, 7-(3,4-dihydro)-1H-thiopyrano[4,3-c]pyridinyl, 7-(3,4-dihydro)-2H-thiopyrano[3,2-c]pyridinyl,
- 25 5-(3,4-dihydro)-2H-thiopyrano[3,2-c]pyridinyl, 5-(3,4-dihydro)-1H-thiopyrano[4,3-c]pyridinyl, 8-(3,4-dihydro)-1H-thiopyrano[3,4-c]pyridinyl, 8-(3,4-dihydro)-2H-thiopyrano[2,3-c]pyridinyl, 7-(3,4-dihydro)-2H-thiopyrano[2,3-b]pyridinyl, 2-(5,6-dihydro)-1H-thiopyrano[3,4-b]pyridinyl, 2-(5,6-dihydro)-2H-thiopyrano[4,3-b]pyridinyl, 6-(3,4-dihydro)-2H-thiopyrano[3,2-b]pyridinyl, 5-benzo[b]thiophenyl, 4-
- 30 benzo[b]thiophenyl, 6-benzo[b]thiophenyl, 7-benzo[b]thiophenyl, 5-(2,3-dihydro)-benzo[b]thiophenyl, 4-(2,3-dihydro)-benzo[b]thiophenyl, 6-(2,3-dihydro)-benzo[b]thiophenyl, 7-(2,3-dihydro)-benzo[b]thiophenyl, 4-(1,3-dihydro)-benzo[c]thiophenyl, 5-(1,3-dihydro)-benzo[c]thiophenyl, 5-(3,4-dihydro)-1H-2-benzothiopyranyl, 6-(3,4-dihydro)-1H-2-benzothiopyranyl, 7-(3,4-dihydro)-1H-2-
- 35 benzothiopyranyl, 8-(3,4-dihydro)-1H-2-benzothiopyranyl, 5-(3,4-dihydro)-2H-1-benzothiopyranyl, 6-(3,4-dihydro)-2H-1-benzothiopyranyl, 7-(3,4-dihydro)-2H-1-

benzothiopyranyl, 8-(3,4-dihydro)-2H-1-benzothiopyranyl;

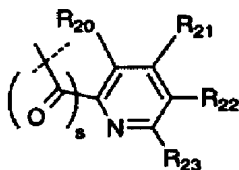
or a member selected from the group consisting of: 4-quinolinyl, 5-quinolinyl, 6-quinolinyl, 7-quinolinyl, 8-quinolinyl, 1-cyclohexenyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 2-imidazolyl, 4-imidazolyl, 2-benzothiazolyl, 2-benzoxazolyl, 2-benzimidazolyl, 2-oxazolyl, 4-oxazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 5-methyl-3-isoxazolyl, 5-phenyl-3-isoxazolyl, 4-thiazolyl, 3-methyl-2-pyrazinyl, 5-methyl-2-pyrazinyl, 6-methyl-2-pyrazinyl, 5-chloro-2-thienyl, 3-furyl, benzofuran-2-yl, benzothien-2-yl, 2H-1-benzopyran-3-yl, 2,3-dihydrobenzopyran-5-yl, 2,3-dihydrobenzofuran-2-yl, 1-methylimidazol-2-yl, quinoxalin-2-yl, isoquinolin-3-yl, piperon-5-yl, 4,7-dichlorobenzoxazol-2-yl, 4,6-dimethylpyrimidin-2-yl, 4-methylpyrimidin-2-yl, 2,4-dimethylpyrimidin-6-yl, 2-methylpyrimidin-4-yl, 4-methylpyrimidin-6-yl, 6-chloropiperon-5-yl, 5-chloroimidazo[1,2-a]pyridin-2-yl, 1-H-inden-3-yl, 1-H-2-methyl-inden-2-yl, 3,4-dihydronaphth-1-yl, S-4-isopropenyl-cyclohexen-1-yl and 4-dihydronaphth-2-yl.

Preferred thioalkyl-substituted pyrimidine-2-thioalkyl and alkylether anti-AIDS compounds of Formula I include compounds where Y is S, and m is 0.

Additional preferred thioalkyl substituted pyrimidine-2-thioalkyl and alkylether anti-AIDS compounds of Formula I include compounds where Y is S, m is 0, R₁₂ is CH₃ and R₁₃ is -H.

Additional preferred thio-substituted pyrimidine-2-thioalkyl and alkylether anti-AIDS compounds of Formula I include compounds where Y is S, m is 0, R₁₂ is CH₃, R₁₃ is -H, R₄ is NH₂, R₅ is -H and R₆ is -S-CH₃.

More preferred thioalkyl substituted pyrimidine-2-thioalkyl and alkylether anti-AIDS compounds of Formula I include compounds where Y is S, m is 0, s is 0, R₁₂ is CH₃, R₁₃ is -H, R₄ is NH, R₅ is -H, R₆ is -S-CH₃, and R₁ is selected from the group consisting of



Most preferred thioalkyl substituted pyrimidine-2-thioalkyl and alkylether anti-AIDS compounds of Formula I include compounds where Y is S, m is 0, s is 0, R₁₂ is CH₃, R₁₃ is -H, R₄ is NH₂, R₅ is -H, R₆ is -S-CH₃, and R₁ is selected from the group consisting of 3-isoquinolinyl, 1-isoquinolinyl, 2-quinolinyl, 3-quinolinyl, 3-

- (5,6,7,8-tetrahydro)-isoquinoliny, 1-(5,6,7,8-tetrahydro)-isoquinoliny, 2-(5,6,7,8-tetrahydro)-quinoliny, 3-(5,6,7,8-tetrahydro)-quinoliny, 3-(5,6-dihydro)-2H-2-pyrindiny, 1-(5,6-dihydro)-2H-2-pyrindiny, 2-(5,6-dihydro)-1H-1-pyrindiny, 3-(5,6-dihydro)-1H-1-pyrindiny, 5-furo[2,3-c]pyridiny, 6-furo[3,2-c]pyridiny, 4-furo[3,2-c]pyridiny, 7-furo[2,3-c]pyridiny, 6-furo[2,3-b]pyridiny, 5-furo[3,2-b]pyridiny, 5-(2,3-dihydro)-furo[2,3-c]pyridiny, 6-(2,3-dihydro)-furo[3,2-c]pyridiny, 4-(2,3-dihydro)-furo[3,2-c]pyridiny, 7-(2,3-dihydro)-furo[2,3-c]pyridiny, 6-(2,3-dihydro)-furo[2,3-b]pyridiny, 5-(2,3-dihydro)-furo[3,2-b]pyridiny, 6-(1,3-dihydro)-furo[3,4-c]pyridiny, 4-(1,3-dihydro)-furo[3,4-c]pyridiny, 2-(5,7-dihydro)-furo[3,4-b]pyridiny, 6-(3,4-dihydro)-2H-pyrano[2,3-c]pyridiny, 6-(3,4-dihydro)-1H-pyrano[3,4-c]pyridiny, 7-(3,4-dihydro)-1H-pyrano[4,3-c]pyridiny, 7-(3,4-dihydro)-2H-pyrano[3,2-c]pyridiny, 5-(3,4-dihydro)-2H-pyrano[3,2-c]pyridiny, 5-(3,4-dihydro)-1H-pyrano[4,3-c]pyridiny, 8-(3,4-dihydro)-1H-pyrano[3,4-c]pyridiny, 8-(3,4-dihydro)-2H-pyrano[2,3-c]pyridiny, 7-(3,4-dihydro)-2H-pyrano[2,3-b]pyridiny, 2-(5,6-dihydro)-1H-pyrano[3,4-b]pyridiny, 2-(5,6-dihydro)-2H-pyrano[4,3-b]pyridiny, 6-(3,4-dihydro)-2H-pyrano[3,2-b]pyridiny, 5-1H-pyrrolo[2,3-c]pyridiny, 6-1H-pyrrolo[3,2-c]pyridiny, 4-1H-pyrrolo[3,2-c]pyridiny, 7-1H-pyrrolo[2,3-c]pyridiny, 6-1H-pyrrolo[2,3-b]pyridiny, 5-1H-pyrrolo[3,2-b]pyridiny, 5-(2,3-dihydro)-1H-pyrrolo[2,3-c]pyridiny, 6-(2,3-dihydro)-1H-pyrrolo[3,2-c]pyridiny, 4-(2,3-dihydro)-1H-pyrrolo[3,2-c]pyridiny, 7-(2,3-dihydro)-1H-pyrrolo[2,3-c]pyridiny, 6-(2,3-dihydro)-1H-pyrrolo[2,3-b]pyridiny, 5-(2,3-dihydro)-1H-pyrrolo[3,2-b]pyridiny, 6-(1,3-dihydro)-1H-pyrrolo[3,4-c]pyridiny, 4-(1,3-dihydro)-1H-pyrrolo[3,4-c]pyridiny, 2-(5,7-dihydro)-1H-pyrrolo[3,4-b]pyridiny, 6-1,7-naphthyridiny, 6-2,7-naphthyridiny, 7-2,6-naphthyridiny, 7-1,6-naphthyridiny, 5-1,6-naphthyridiny, 5-2,6-naphthyridiny, 8-2,7-naphthyridiny, 8-1,7-naphthyridiny, 7-1,8-naphthyridiny, 2-1,7-naphthyridiny, 2-1,6-naphthyridiny, 6-1,5-naphthyridiny, 6-(1,2,3,4-tetrahydro)-1,7-naphthyridiny, 6-(1,2,3,4-tetrahydro)-2,7-naphthyridiny, 7-(1,2,3,4-tetrahydro)-2,6-naphthyridiny, 7-(1,2,3,4-tetrahydro)-1,6-naphthyridiny, 5-(1,2,3,4-tetrahydro)-1,6-naphthyridiny, 5-(1,2,3,4-tetrahydro)-2,6-naphthyridiny, 8-(1,2,3,4-tetrahydro)-2,7-naphthyridiny, 8-(1,2,3,4-tetrahydro)-1,7-naphthyridiny, 7-(1,2,3,4-tetrahydro)-1,8-naphthyridiny, 2-(5,6,7,8-tetrahydro)-1,7-naphthyridiny, 2-(5,6,7,8-tetrahydro)-1,6-naphthyridiny, 6-(1,2,3,4-tetrahydro)-1,5-naphthyridiny, 1-naphthyl, 2-naphthyl, 5-(1,2,3,4-tetrahydro)-naphthyl, 6-(1,2,3,4-tetrahydro)-naphthyl, 4-(2,3-dihydro)-1H-indenyl, 5-(2,3-dihydro)-1H-indenyl, 5-benzofuranyl, 4-benzofuranyl, 6-benzofuranyl, 7-benzofuranyl, 5-(2,3-dihydro)-benzofuranyl, 4-(2,3-dihydro)-benzofuranyl, 6-(2,3-dihydro)-benzofuranyl, 7-(2,3-dihydro)-benzofuranyl, 4-(1,3-dihydro)-isobenzofuran, 5-(1,3-dihydro)-isobenzofuran, 4-1H-indolyl, 5-1H-indolyl, 6-

1H-indolyl, 7-1H-indolyl, 4-(2,3-dihydro)-1H-indolyl, 5-(2,3-dihydro)-1H-indolyl, 6-(2,3-dihydro)-1H-indolyl, 7-(2,3-dihydro)-1H-indolyl, 4-(1,3-dihydro)-1H-isoindolyl, 5-(1,3-dihydro)-1H-isoindolyl, 5-(3,4-dihydro)-1H-2-benzopyranyl, 6-(3,4-dihydro)-1H-2-benzopyranyl, 7-(3,4-dihydro)-1H-2-benzopyranyl, 8-(3,4-dihydro)-1H-2-benzopyranyl, 5-(3,4-dihydro)-2H-1-benzopyranyl, 6-(3,4-dihydro)-2H-1-benzopyranyl, 7-(3,4-dihydro)-2H-1-benzopyranyl, 8-(3,4-dihydro)-2H-1-benzopyranyl, 5-(1,2,3,4-tetrahydro)-isoquinolinyl, 6-(1,2,3,4-tetrahydro)-isoquinolinyl, 7-(1,2,3,4-tetrahydro)-isoquinolinyl, 8-(1,2,3,4-tetrahydro)-isoquinolinyl, 5-(1,2,3,4-tetrahydro)-quinolinyl, 6-(1,2,3,4-tetrahydro)-quinolinyl, 7-(1,2,3,4-tetrahydro)-quinolinyl, 8-(1,2,3,4-tetrahydro)-quinolinyl, 5-thieno[2,3-c]pyridinyl, 6-thieno[3,2-c]pyridinyl, 4-thieno[3,2-c]pyridinyl, 7-thieno[2,3-c]pyridinyl, 6-thieno[2,3-b]pyridinyl, 5-thieno[3,2-b]pyridinyl, 5-(2,3-dihydro)-thieno[2,3-c]pyridinyl, 6-(2,3-dihydro)-thieno[3,2-c]pyridinyl, 4-(2,3-dihydro)-thieno[3,2-c]pyridinyl, 7-(2,3-dihydro)-thieno[2,3-c]pyridinyl, 6-(2,3-dihydro)-thieno[2,3-b]pyridinyl, 5-(2,3-dihydro)-thieno[3,2-b]pyridinyl, 6-(1,3-dihydro)-thieno[3,4-c]pyridinyl, 4-(1,3-dihydro)-thieno[3,4-c]pyridinyl, 2-(5,7-dihydro)-thieno[3,4-b]pyridinyl, 6-(3,4-dihydro)-2H-thiopyrano[2,3-c]pyridinyl, 6-(3,4-dihydro)-1H-thiopyrano[3,4-c]pyridinyl, 7-(3,4-dihydro)-1H-thiopyrano[4,3-c]pyridinyl, 7-(3,4-dihydro)-2H-thiopyrano[3,2-c]pyridinyl, 5-(3,4-dihydro)-2H-thiopyrano[3,2-c]pyridinyl, 5-(3,4-dihydro)-1H-thiopyrano[4,3-c]pyridinyl, 8-(3,4-dihydro)-1H-thiopyrano[3,4-c]pyridinyl, 8-(3,4-dihydro)-2H-thiopyrano[2,3-c]pyridinyl, 7-(3,4-dihydro)-2H-thiopyrano[2,3-b]pyridinyl, 2-(5,6-dihydro)-1H-thiopyrano[3,4-b]pyridinyl, 2-(5,6-dihydro)-2H-thiopyrano[4,3-b]pyridinyl, 6-(3,4-dihydro)-2H-thiopyrano[3,2-b]pyridinyl, 5-benzo[b]thiophenyl, 4-benzo[b]thiophenyl, 6-benzo[b]thiophenyl, 7-benzo[b]thiophenyl, 5-(2,3-dihydro)-benzo[b]thiophenyl, 4-(2,3-dihydro)-benzo[b]thiophenyl, 6-(2,3-dihydro)-benzo[b]thiophenyl, 7-(2,3-dihydro)-benzo[b]thiophenyl, 4-(1,3-dihydro)-benzo[c]thiophenyl, 5-(1,3-dihydro)-benzo[c]thiophenyl, 5-(3,4-dihydro)-1H-2-benzothiopyranyl, 6-(3,4-dihydro)-1H-2-benzothiopyranyl, 7-(3,4-dihydro)-1H-2-benzothiopyranyl, 8-(3,4-dihydro)-1H-2-benzothiopyranyl, 5-(3,4-dihydro)-2H-1-benzothiopyranyl, 6-(3,4-dihydro)-2H-1-benzothiopyranyl, 7-(3,4-dihydro)-2H-1-benzothiopyranyl, 8-(3,4-dihydro)-2H-1-benzothiopyranyl;

most preferably a member selected from the group consisting of:

3-isoquinolinyl, 1-isoquinolinyl, 2-quinolinyl, 3-quinolinyl, 3-(5,6,7,8-tetrahydro)-isoquinolinyl, 1-(5,6,7,8-tetrahydro)-isoquinolinyl, 2-(5,6,7,8-tetrahydro)-quinolinyl, 3-(5,6,7,8-tetrahydro)-quinolinyl, 3-(5,6-dihydro)-2H-2-pyrindinyl, 1-(5,6-dihydro)-2H-2-pyrindinyl, 2-(5,6-dihydro)-1H-1-pyrindinyl, 3-(5,6-dihydro)-1H-1-pyrindinyl, 5-

furo[2,3-c]pyridinyl, 6-furo[3,2-c]pyridinyl, 4-furo[3,2-c]pyridinyl, 7-furo[2,3-c]pyridinyl, 6-furo[2,3-b]pyridinyl, 5-furo[3,2-b]pyridinyl, 5-(2,3-dihydro)-furo[2,3-c]pyridinyl, 6-(2,3-dihydro)-furo[3,2-c]pyridinyl, 4-(2,3-dihydro)-furo[3,2-c]pyridinyl, 7-(2,3-dihydro)-furo[2,3-c]pyridinyl, 6-(2,3-dihydro)-furo[2,3-b]pyridinyl, 5-(2,3-dihydro)-furo[3,2-b]pyridinyl, 6-(1,3-dihydro)-furo[3,4-c]pyridinyl, 4-(1,3-dihydro)-furo[3,4-c]pyridinyl, 2-(5,7-dihydro)-furo[3,4-b]pyridinyl, 6-(3,4-dihydro)-2H-pyrano[2,3-c]pyridinyl, 6-(3,4-dihydro)-1H-pyrano[3,4-c]pyridinyl, 7-(3,4-dihydro)-1H-pyrano[4,3-c]pyridinyl, 7-(3,4-dihydro)-2H-pyrano[3,2-c]pyridinyl, 5-(3,4-dihydro)-2H-pyrano[3,2-c]pyridinyl, 5-(3,4-dihydro)-1H-pyrano[4,3-c]pyridinyl, 8-(3,4-dihydro)-1H-pyrano[3,4-c]pyridinyl, 8-(3,4-dihydro)-2H-pyrano[2,3-c]pyridinyl, 7-(3,4-dihydro)-2H-pyrano[2,3-b]pyridinyl, 2-(5,6-dihydro)-1H-pyrano[3,4-b]pyridinyl, 2-(5,6-dihydro)-2H-pyrano[4,3-b]pyridinyl, 6-(3,4-dihydro)-2H-pyrano[3,2-b]pyridinyl.

The 6-thioalkyl pyrimidine-2-thioalkyl compounds of Formula I are generally and most often prepared by contacting a 6-chloro pyrimidine-2-thioalkyl compound of Formula I with an appropriate alkyl thiolate, e.g. sodium thiomethoxide, sodium thioethoxide, etc. (Chart A)

Alternatively, the 6-thioalkyl pyrimidine 2-thioalkyl compounds of Formula I are prepared by contacting a 6-thioalkyl-2-thiopyrimidine with an appropriate alkylating agent, e.g. mesylate or halide. The corresponding 6-thioalkyl-2-thiopyrimidine is prepared by, for example, by reacting 4-amino-6-chloro-2-(4-methoxybenzyl)thiopyrimidine with an appropriate alkyl thiolate followed by deprotection with an appropriate reagent such as methane sulfonic acid. (Chart B)

When R_{12} and R_{13} are different, the compounds of Formula I are drawn as the racemic mixture and include the R and S isomers, which can be resolved from the racemic mixture by HPLC using a chiral column, such as Chiralcel OD-H, eluting with an appropriate solvent mixture, such as isopropanol/hexane. The R and S isomers of Formula I (when R_{12} and R_{13} are different) can be prepared from an appropriate chiral halide (or mesylate) II (see Chart B). The appropriate chiral halide (or mesylate) II is prepared from a chiral alcohol IV. The appropriate chiral alcohol IV can be prepared from the appropriate ketone V using a chiral reducing agent, such as (+) or (-)-diisopinocampheylchloroborane or other chiral reducing agents known in the art. The appropriate chiral alcohol IV is also obtained from the resolution of the racemic alcohol VII via the enzymatic hydrolysis of the appropriate racemic acetate VI with the appropriate enzyme, such as PS-30 amano lipase or L1754 Type VII from candidae cylindracea or other enzymes known in the art. The appropriate chiral alcohol IV is also obtained from the resolution of the racemic

alcohol VII via the enzymatic esterification (such as acetylation or butyration) of the racemic alcohol VII (to give chiral VIII) using the appropriate enzyme, such as porcine pancreatic lipase type II, or other enzymes known in the art.

The 6-thioalkyl substituted pyrimidine-2-thioalkyl and alkylether compounds
5 of Formula I include the compounds of EXAMPLES 1-304. Preferred are the anti-AIDS compounds of EXAMPLES 230, 231, 233, 234, 237, 238, 239, 240, 241, 242, 243, 246, 247, 248, 249, 250, 251, 252, 256, 269, 270, 271, 272, 273, 277, 194, 199, 203, 207, 282, 283, 284, 285, 286, 287, 289, 290, 297, 1 and preferably 237, 238, 239, 246, 289, 290, 297, 1 and more preferably 290, 297, 1 and salts thereof (e.g.
10 302, 306 and 301).

The pyrimidine-thioalkyl and alkylether compounds of Formula I form acid addition salts; such as mesylate, hydrochloride, hydrobromide, hydroiodide, sulfate, phosphate, acetate, propionate, lactate, maleate, malate, succinate, tartrate, and the like. Some of the variable substituents are acids and as such form base addition
15 salts when reacted with bases of sufficient strength. The pharmaceutically acceptable salts include both inorganic and organic bases. The preferred pharmaceutically acceptable salts include salts of the following bases, for example, hydroxide, ammonia, tromethamine (THAM), 2-amino-2-(hydroxymethyl)-1,3-propanediol. Suitable cations include, for example, sodium, potassium, calcium and magnesium.

20 The pyrimidine-thioalkyl and alkylether anti-AIDS compounds of Formula I are useful as inhibitors of viral reverse transcriptase, an enzyme necessary for human immunodeficiency virus replication and therefore would be useful in the treatment of such diseases as AIDS.

The term human retrovirus (HRV) indicates human immunodeficiency virus
25 type I, or strains thereof apparent to one skilled in the art, which belong to the same viral families and which create similar physiological effects in humans as various human retroviruses.

Patients to be treated would include those individuals (1) infected with one or more than one strain of a human retrovirus as determined by the presence of either
30 measurable viral antibody or antigen in the serum and (2) having either a symptomatic AIDS defining infection such as (a) disseminated histoplasmosis, (b) isopsoriasis, (c) bronchial and pulmonary candidiasis including pneumocystic pneumonia (d) non-Hodgkin's lymphoma or (e) Kaposi's sarcoma and being less than sixty years old; or having an absolute CD4 lymphocyte count of less than $200/\text{mm}^3$ in the
35 peripheral blood.

The compounds of Formula I can be given orally. Suitable dosage forms

include tablets, capsules, suspensions, solutions and elixirs. An effective amount is from about 0.1 to about 500 mg/kg/day. A typical unit dose for a 70 kg human would be from about 10 mg to about 2000 mg, preferably about 100 mg to about 1000 mg taken one to six times per day.

5 The exact dosage and frequency of administration depends on the particular compound of Formula I used, the particular condition being treated, the severity of the condition being treated, the age, weight, general physical condition of the particular patient, other medication the individual may be taking as is well known to those skilled in the art and can be more accurately determined by measuring the
10 blood level or concentration of the compounds of Formula I in the patient's blood and/or the patient's response to the particular condition being treated.

 Patients who are HIV positive but asymptomatic would typically be treated with lower oral doses (about 0.2 to about 100 mg/kg/day. ARC (AIDS-related complex) and AIDS patients would typically be treated with higher oral doses (about
15 1 to about 500 mg/kg/day).

 The pyrimidine-thioalkyl and alkylether anti-AIDS compounds of Formula I of this invention can be used in conjunction with (or sequentially with) other antiviral agents such as AZT, ddI, ddC, 3TC, d4T, with non-nucleoside anti-AIDS agents such as those disclosed in Serial No. 08/400,095 Case 4788.1 CP, filed March
20 7, 1995, International Publication No. WO91/09849, published July 11, 1991, and International Publication No. WO93/01181, published January 21, 1993, and with protease inhibitors.

 The utility of the pyrimidine-thioalkyl and alkylether anti-AIDS compounds of Formula I of this invention can be determined by their ability to inhibit viral
25 reverse transcriptase, an enzyme essential for human immunodeficiency virus replication. This enzyme has characteristics which differentiate it from other known cellular polymerases and it is a unique enzyme which is not found in uninfected cells. Viral reverse transcriptase (Wild Type) is found in extracts from bacterial clones prepared according to the procedure described in AIDS Virus Reverse
30 Transcriptase defined by high level expression in Escherichia coli, EMBO J. 6:3133-3137 (1987). P236L viral reverse transcriptase is obtained by PNAS 90: 4713-4717 (1993). Inhibition of this enzyme is determined in a cell free assay which measures the level of radioactive precursors incorporated into DNA.

 Assessment of the antiviral activities of the Compounds 1 and 290 versus the
35 panel of viruses used in these studies was carried out in MT4 cells. Cells were batch infected with the appropriate virus stock at a multiplicity of infection of 0.001-

0.005 TCID₅₀ per cell for 2 hours at 37°C. The cells were washed, resuspended in RPMI/FBS and plated in 24 well dishes at a final concentration of 1.5×10^5 cells/ml to which were added 2X drug treatments prepared in RPMI/FBS. All treatment concentrations were tested in duplicate. The final DMSO concentration for all treatments or vehicle control cultures was 0.1%. At four days post-infection culture fluid samples were collected for HIV-1 p24 core antigen quantitation to determine antiviral effects. Linear regression analysis was used to calculate the drug concentration necessary to inhibit 90% (inhibitory concentration 90, IC₉₀) of non-drug treated p24 antigen production.

RTI	MF-delavirdine (P236L)	IIIB-WT
	IC ₉₀ (μM)	IC ₉₀ (μM)
Compound #1	0.02	0.008
Compound #290	0.02	0.004

15

DEFINITIONS AND CONVENTIONS

The definitions and explanations below are for the terms as used throughout this entire document including both the specification and the claims.

I. CONVENTIONS FOR FORMULAS AND DEFINITIONS OF VARIABLES

The chemical formulas representing various compounds or molecular fragments in the specification and claims may contain variable substituents in addition to expressly defined structural features. These variable substituents are identified by a letter or a letter followed by a numerical subscript, for example, "Z_i" or "R_i" where "i" is an integer. These variable substituents are either monovalent or bivalent, that is, they represent a group attached to the formula by one or two chemical bonds. For example, a group Z₁ would represent a bivalent variable if attached to the formula CH₃-C(=Z₁)H. Groups R_i and R_j would represent monovalent variable substituents if attached to the formula CH₃-CH₂-C(R_i)(R_j)H. When chemical formulas are drawn in a linear fashion, such as those above, variable substituents contained in parentheses are bonded to the atom immediately to the left of the variable substituent enclosed in parenthesis. When two or more consecutive variable substituents are enclosed in parentheses, each of the consecutive variable substituents is bonded to the immediately preceding atom to the left which is not enclosed in parentheses. Thus, in the formula above, both R_i and R_j are bonded to

the preceding carbon atom.

Chemical formulas or portions thereof drawn in a linear fashion represent atoms in a linear chain. The symbol "-" in general represents a bond between two atoms in the chain. Thus $\text{CH}_3\text{-O-CH}_2\text{-CH(R}_1\text{)-CH}_3$ represents a 2-substituted-1-methoxypropane compound. In a similar fashion, the symbol "=" represents a double bond, e.g., $\text{CH}_2=\text{C(R}_1\text{)-O-CH}_3$, and the symbol " \equiv " represents a triple bond, e.g., $\text{HC}\equiv\text{C-CH(R}_1\text{)-CH}_2\text{-CH}_3$. Carbonyl groups are represented in either one of two ways: -CO- or -C(=O)- , with the former being preferred for simplicity.

Chemical formulas of cyclic (ring) compounds or molecular fragments can be represented in a linear fashion. Thus, the compound 4-chloro-2-methylpyridine can be represented in linear fashion by $\text{N}^*=\text{C(CH}_3\text{)-CH=}\ddot{\text{C}}\text{Cl-CH=C}^*\text{H}$ with the convention that the atoms marked with an asterisk (*) are bonded to each other resulting in the formation of a ring. Likewise, the cyclic molecular fragment, 4-(ethyl)-1-piperazinyl can be represented by $\text{-N}^*\text{-(CH}_2\text{)}_2\text{-N(C}_2\text{H}_5\text{)-CH}_2\text{-C}^*\text{H}_2$.

A rigid cyclic (ring) structure for any compounds herein defines an orientation with respect to the plane of the ring for substituents attached to each carbon atom of the rigid cyclic compound. For saturated compounds which have two substituents attached to a carbon atom which is part of a cyclic system, $\text{-C(X}_1\text{)(X}_2\text{)-}$ the two substituents may be in either an axial or equatorial position relative to the ring and may change between axial/equatorial. However, the position of the two substituents relative to the ring and each other remains fixed. While either substituent at times may lie in the plane of the ring (equatorial) rather than above or below the plane (axial), one substituent is always above the other. In chemical structural formulas depicting such compounds, a substituent (X_1) which is "below" another substituent (X_2) will be identified as being in the alpha (α) configuration and is identified by a broken, dashed or dotted line attachment to the carbon atom, i.e., by the symbol "- - -" or "...". The corresponding substituent attached "above" (X_2) the other (X_1) is identified as being in the beta (β) configuration and is indicated by an unbroken line attachment to the carbon atom.

When a variable substituent is bivalent, the valences may be taken together or separately or both in the definition of the variable. For example, a variable R_i attached to a carbon atom as $\text{-C(=R}_i\text{)-}$ might be bivalent and be defined as oxo or keto (thus forming a carbonyl group (-CO-)) or as two separately attached monovalent variable substituents $\alpha\text{-R}_{i-j}$ and $\beta\text{-R}_{i-k}$. When a bivalent variable, R_i , is defined to consist of two monovalent variable substituents, the convention used to define the bivalent variable is of the form " $\alpha\text{-R}_{i-j}:\beta\text{-R}_{i-k}$ " or some variant thereof. In such a

case both $\alpha\text{-R}_{i-j}$ and $\beta\text{-R}_{i-k}$ are attached to the carbon atom to give $-\text{C}(\alpha\text{-R}_{i-j})(\beta\text{-R}_{i-k})-$. For example, when the bivalent variable R_6 , $-\text{C}(=\text{R}_6)-$ is defined to consist of two monovalent variable substituents, the two monovalent variable substituents are $\alpha\text{-R}_{6-1}:\beta\text{-R}_{6-2}$, ..., $\alpha\text{-R}_{6-9}:\beta\text{-R}_{6-10}$, etc, giving $-\text{C}(\alpha\text{-R}_{6-1})(\beta\text{-R}_{6-2})-$, ..., $-\text{C}(\alpha\text{-R}_{6-9})(\beta\text{-R}_{6-10})-$, etc. Likewise, for the bivalent variable R_{11} , $-\text{C}(=\text{R}_{11})-$, two monovalent variable substituents are $\alpha\text{-R}_{11-1}:\beta\text{-R}_{11-2}$. For a ring substituent for which separate α and β orientations do not exist (e.g., due to the presence of a carbon double bond in the ring), and for a substituent bonded to a carbon atom which is not part of a ring the above convention is still used, but the α and β designations are omitted.

Just as a bivalent variable may be defined as two separate monovalent variable substituents, two separate monovalent variable substituents may be defined to be taken together to form a bivalent variable. For example, in the formula $-\text{C}_1(\text{R}_i)\text{H}-\text{C}_2(\text{R}_j)\text{H}-$ (C_1 and C_2 define arbitrarily a first and second carbon atom, respectively) R_i and R_j may be defined to be taken together to form (1) a second bond between C_1 and C_2 or (2) a bivalent group such as oxa ($-\text{O}-$) and the formula thereby describes an epoxide. When R_i and R_j are taken together to form a more complex entity, such as the group $-\text{X}-\text{Y}-$, then the orientation of the entity is such that C_1 in the above formula is bonded to X and C_2 is bonded to Y. Thus, by convention the designation "... R_i and R_j are taken together to form $-\text{CH}_2-\text{CH}_2-\text{O}-\text{CO}-$..." means a lactone in which the carbonyl is bonded to C_2 . However, when designated "... R_j and R_i are taken together to form $-\text{CO}-\text{O}-\text{CH}_2-\text{CH}_2-$ the convention means a lactone in which the carbonyl is bonded to C_1 .

The carbon atom content of variable substituents is indicated in one of two ways. The first method uses a prefix to the entire name of the variable such as " $\text{C}_1\text{-C}_4$ ", where both "1" and "4" are integers representing the minimum and maximum number of carbon atoms in the variable. The prefix is separated from the variable by a space. For example, " $\text{C}_1\text{-C}_4$ alkyl" represents alkyl of 1 through 4 carbon atoms, (including isomeric forms thereof unless an express indication to the contrary is given). Whenever this single prefix is given, the prefix indicates the entire carbon atom content of the variable being defined. Thus $\text{C}_2\text{-C}_4$ alkoxy-carbonyl describes a group $\text{CH}_3-(\text{CH}_2)_n-\text{O}-\text{CO}-$ where n is zero, one or two. By the second method the carbon atom content of only each portion of the definition is indicated separately by enclosing the " $\text{C}_i\text{-C}_j$ " designation in parentheses and placing it immediately (no intervening space) before the portion of the definition being defined. By this optional convention ($\text{C}_1\text{-C}_3$)alkoxy-carbonyl has the same meaning as $\text{C}_2\text{-C}_4$ alkoxy-carbonyl because the " $\text{C}_1\text{-C}_3$ " refers only to the carbon atom content of the alkoxy

group. Similarly while both C₂-C₆ alkoxyalkyl and (C₁-C₃)alkoxy(C₁-C₃)alkyl define alkoxyalkyl groups containing from 2 to 6 carbon atoms, the two definitions differ since the former definition allows either the alkoxy or alkyl portion alone to contain 4 or 5 carbon atoms while the latter definition limits either of these groups to 3 carbon atoms.

When the claims contain a fairly complex (cyclic) substituent, at the end of the phrase naming/designating that particular substituent will be a notation in (parentheses) which will correspond to the same name/designation in one of the CHARTS which will also set forth the chemical structural formula of that particular substituent.

II. DEFINITIONS

All temperatures are in degrees Centigrade.

TLC refers to thin-layer chromatography.

Chromatography refers to medium pressure chromatography on silica gel.

THF refers to tetrahydrofuran.

TBDMS refers to tert-butyldimethylsilyl.

Saline refers to an aqueous saturated sodium chloride solution.

NMR refers to nuclear (proton) magnetic resonance spectroscopy, chemical shifts are reported in ppm (δ) downfield from tetramethylsilane.

IR refers to infrared spectroscopy.

$-\phi$ refers to phenyl (C₆H₅).

MS refers to mass spectrometry expressed as m/e or mass/charge unit. [M + H]⁺ refers to the positive ion of a parent plus a hydrogen atom. EI refers to electron impact. CI refers to chemical ionization. FAB refers to fast atom bombardment.

Ether refers to diethyl ether.

Halo refers to a halogen atom (-Cl, -Br, -F or -I).

Pharmaceutically acceptable refers to those properties and/or substances which are acceptable to the patient from a pharmacological/toxicological point of view and to the manufacturing pharmaceutical chemist from a physical/chemical point of view regarding composition, formulation, stability, patient acceptance and bioavailability.

Pyridinyl refers to the pyridyl radical as defined by IUPAC nomenclature. For example, 2-pyridyl (pyridine ring substituted in the 2-position).

When solvent pairs are used, the ratios of solvents used are volume/volume (v/v).

HIV refers to HIV-1 (wild type and/or drug resistant mutants thereof e.g.

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M41L, K65N, K67L, K70R, L74V, V75T, A98G, L100I, K103E, K103N, K103Q, V106A, V108I, E138K, V179D, V179E, Y181C, Y188H, Y188L, G190A, T215Y, T215F, K219Q, K219E, P236L and K238T).

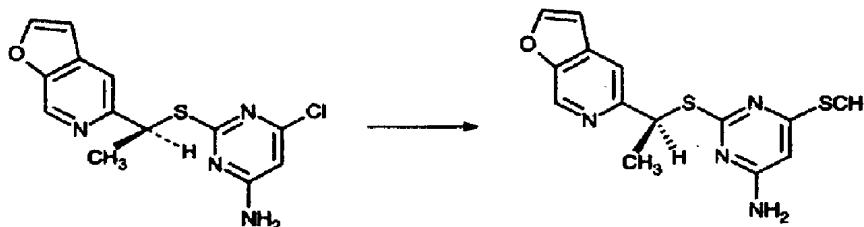
Treatment refers to inhibition of the HIV virus and will differ depending on the infected individual. For individuals who are HIV positive (infected) but who are asymptomatic, the pyrimidine-thioalkyl derivatives of Formula I will delay, or prevent, the onset of symptoms. For individuals who are HIV positive, symptomatic and are pre-AIDS or ARC patients, the pyrimidine-thioalkyl derivatives of Formula I will delay, or prevent, the onset of "full blown AIDS". For individuals who have "full blown AIDS", the pyrimidine-thioalkyl and alkylether derivatives of Formula I will extend survival time of these individuals.

Pyrimidine-thioalkyl and alkylether compounds of Formula I include alpha-substituted pyrimidine-thioalkyl and alkylether compounds. All references to "pyrimidine-thioalkyl and alkylether compounds" and "pyrimidine-thioalkyl and alkylether anti-AIDS compounds" include "alpha-substituted pyrimidine-thioalkyl and alkylether compounds" and "alpha-substituted pyrimidine-thioalkyl and alkylether anti-AIDS compounds" unless specifically indicated otherwise.

EXAMPLES

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, practice the present invention to its fullest extent. The following detailed examples describe how to prepare the various compounds and/or perform the various processes of the invention and are to be construed as merely illustrative, and not limitations of the preceding disclosure in any way whatsoever. Those skilled in the art will promptly recognize appropriate variations from the procedures both as to reactants and as to reaction conditions and techniques.

Example 1: Preparation of (S)-(-)-4-Amino-2-(1-(furo[2,3c]pyridin-5-yl)ethylthio)-6-methylthio-pyrimidine; Compound #1



(S)-(-)-4-Amino-6-chloro-2-(1-(furo[2,3c]pyridin-5-yl)ethyl)thio-pyrimidine (920 mg, 3.0 mmole) is combined with sodium thiomethoxide (263 mg, 3.75 mmole) in 5 ml dimethylformamide in a 25 ml one neck round bottom flask under nitrogen. The reaction is warmed to 65 °C for 45 min, cooled, and is diluted with 25 ml ethyl acetate. The organics are washed with 4 x 25 ml of 50% saturated 1:1 sodium chloride/sodium bicarbonate, are dried over anhydrous potassium carbonate, and are concentrated in vacuo to a pale oil. The crude material is chromatographed over 60 g of silica gel (230-400 mesh), eluting with 45% ethyl acetate/hexane while collecting 9 ml fractions. Fractions 51-92 are combined and concentrated to a pale oil which is crystallized from diethyl ether to afford the title compound as a pale yellow solid.

¹H NMR (d₆DMSO): δ 1.69 (d, J=7 Hz, 3), 2.40 (s, 3), 5.16 (q, J=7, Hz, 1), 5.97 (s, 1), 6.83 (s, 2), 7.00 (m, 1), 7.77 (m, 1), 8.20 (m, 1), 8.87 (s, 1) ppm.

¹³C NMR (d₆DMSO): δ 12.5, 22.5, 45.1, 95.5, 106.8, 114.5, 133.3, 134.8, 150.3, 151.2, 154.9, 162.9, 167.5, 169.3 ppm.

Melting Point: 147-149 °C.

IR (mull): 3427, 3306, 3176, 2375, 2252, 2144, 1996, 1969, 1633, 1556, 1521, 1282, 1270, 1126, 1118 cm⁻¹.

MS (EI) m/z (rel. intensity): 318 (M+, 12), 318 (12), 286 (18), 285 (99), 178 (15), 147 (11), 146 (58), 145 (9), 144 (10), 118 (11), 91 (7).

Specific Rotation (25 °C, D) = -269 ° (c 0.98).

UV λ max: 227(49500, 95% ETHANOL).

Following the general procedure of Example 1 and making noncritical changes, but using the appropriate chloro-pyrimidine, the following compounds are prepared

35	Ex./Cpd #2	4-amino-2-(benzylthio)-6-methylthiopyrimidine
	Ex./Cpd #3	4-amino-2-(2-methylphenylmethylthio)-6-methylthiopyrimidine

	Ex./Cpd #4	4-amino-2-(3-methylphenylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #5	4-amino-2-(4-methylphenylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #6	4-amino-2-(3-trifluoromethylphenylmethylthio)-6-methylthiopyrimidine
5	Ex./Cpd #7	4-amino-2-(3-methoxyphenylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #8	4-amino-2-(4-methoxyphenylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #9	4-amino-2-(3-fluorophenylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #10	4-amino-2-(3-chlorophenylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #11	4-amino-2-(3-bromophenylmethylthio)-6-methylthiopyrimidine
10	Ex./Cpd #12	4-amino-2-(3-iodophenylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #13	4-amino-2-(3-nitrophenylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #14	4-amino-2-(3-carbomethoxyphenylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #15	4-amino-2-(4-t-butylphenylmethylthio)-6-methylthiopyrimidine
15	Ex./Cpd #16	4-amino-2-(3,4-difluorophenylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #17	4-amino-2-(3,4-dichlorophenylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #18	4-amino-2-(3,5-dichlorophenylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #19	4-amino-2-(2,4-dichlorophenylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #20	4-amino-2-(3,5-dibromophenylmethylthio)-6-methylthiopyrimidine
20	Ex./Cpd #21	4-amino-5-cyclohexyl-2-(benzylthio)-6-methylthiopyrimidine
	Ex./Cpd #22	4-amino-5-isopropyl-2-(benzylthio)-6-methylthiopyrimidine
	Ex./Cpd #23	4-amino-2-(2-pyridylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #24	4-amino-2-[2-(3-ethoxy)pyridylmethylthio]-6-methylthiopyrimidine
	Ex./Cpd #25	4-amino-2-(3-pyridylmethylthio)-6-methylthiopyrimidine
25	Ex./Cpd #26	4-amino-2-(1-naphthylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #27	4-amino-2-(2-naphthylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #28	4-amino-2-(6,7-difluoro-2-naphthylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #29	4-amino-2-(2-quinolinylnmethylthio)-6-methylthiopyrimidine
30	Ex./Cpd #30	4-amino-2-(6-chloro-5-piperonylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #32	4-amino-2-(E-styrylmethylthio)-6-methylthiopyrimidine
	Ex./Cpd #33	4-amino-2-(propargylthio)-6-methylthiopyrimidine
	Ex./Cpd #34	4-amino-6-methylthio-2-(2,6-difluorophenylmethylthio)-pyrimidine
	Ex./Cpd #35	4-amino-6-methylthio-2-(3-bromophenylmethylsulfinyl)-pyrimidine
35	Ex./Cpd #36	4-amino-6-methylthio-2-(2-naphthylmethylsulfinyl)-pyrimidine
	Ex./Cpd #37	4-amino-6-methylthio-2-(3-bromophenylmethylsulfonyl)-pyrimidine

	Ex./Cpd #38	4-amino-5-bromo-6-methylthio-2-(2-naphthylmethylthio)-pyrimidine
	Ex./Cpd #39	4-amino-5-bromo-6-methylthio-2-(2-pyridylmethylthio)-pyrimidine
	Ex./Cpd #78	4-chloro-6-methylthio-2-(benzylthio)-pyrimidine
	Ex./Cpd #79	4-chloro-6-methylthio-5-methoxy-2-(2-naphthylmethylthio)-
5		pyrimidine
	Ex./Cpd #80	4-chloro-5-fluoro-6-methylthio-2-(2-naphthylmethylthio)-pyrimidine
	Ex./Cpd #81	4-chloro-5-methyl-6-methylthio-2-(2-naphthylmethylthio)-pyrimidine
	Ex./Cpd #82	4-chloro-5-fluoro-6-methylthio-2-(2-pyridylmethylthio)-pyrimidine
	Ex./Cpd #83	4-chloro-6-methylthio-2-(4-methoxyphenylmethylthio)-pyrimidine
10	Ex./Cpd #84	4-piperido-6-methylthio-2-(benzylthio)-pyrimidine
	Ex./Cpd #85	4-pyrrolidino-6-methylthio-2-(benzylthio)-pyrimidine
	Ex./Cpd #86	4-morpholino-6-methylthio-2-(benzylthio)-pyrimidine
	Ex./Cpd #87	4-propylamino-6-methylthio-2-(benzylthio)-pyrimidine
	Ex./Cpd #88	4-hydrazino-6-methylthio-2-(benzylthio)-pyrimidine
15	Ex./Cpd #89	4-amino-5-methoxy-6-methylthio-2-(2-naphthylmethylthio)-
		pyrimidine
	Ex./Cpd #90	4-amino-5-methyl-6-methylthio-2-(2-naphthylmethylthio)-pyrimidine
	Ex./Cpd #91	4-amino-5-fluoro-6-methylthio-2-(2-naphthylmethylthio)-pyrimidine
	Ex./Cpd #92	4-amino-5-fluoro-6-methylthio-2-(2-pyridylmethylthio)-pyrimidine
20	Ex./Cpd #93	4-amino-6-methylthio-2-(4-methoxyphenylmethylthio)-pyrimidine
	Ex./Cpd #99	4-amino-6-methylthio-2-(2-benzothiazolomethylthio)-pyrimidine
	Ex./Cpd #100	4-amino-6-methylthio-2-[2-(1-phenyl-1-ethanon)thio]-pyrimidine
	Ex./Cpd #101	4-amino-6-methylthio-2-(cyclohex-1-enylmethylthio)-pyrimidine
	Ex./Cpd #102	4-amino-6-methylthio-2-(Z-styrylthio)-pyrimidine
25	Ex./Cpd #103	4-amino-6-methylthio-2-(1-naphthylmethyloxy)-pyrimidine;
	Ex./Cpd #104	4-amino-6-methylthio-2-(benzyloxy)-pyrimidine
	Ex./Cpd #105	4-amino-6-methylthio-2-(2-naphthylmethyloxy)-pyrimidine
	Ex./Cpd #106	4-amino-6-methylthio-2-(3-methylphenylmethyloxy)-pyrimidine
	Ex./Cpd #107	4-amino-6-methylthio-2-(3-bromophenylmethyloxy)-pyrimidine
30	Ex./Cpd #108	4-amino-6-methylthio-2-(3-hydroxyphenylmethylthio)-pyrimidine
	Ex./Cpd #109	4-amino-6-methylthio-2-(3-isopropoxyphenylmethylthio)-pyrimidine
	Ex./Cpd #110	4-amino-6-methylthio-2-thio-pyrimidine
	Ex./Cpd #111	4-amino-6-methylthio-2-[2-(4-chloro)-pyridylmethylthio]-pyrimidine
	Ex./Cpd #112	4-amino-6-methylthio-2-[2-(6-chloro)pyridylmethylthio]-pyrimidine
35	Ex./Cpd #113	4-amino-6-methylthio-2-[2-(6-methyl)pyridylmethylthio]-pyrimidine
	Ex./Cpd #114	4-amino-6-methylthio-2-[2-(4-methyl)pyridylmethylthio]-pyrimidine

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	Ex./Cpd #115	4-amino-6-methylthio-2-[2-(4-ethoxy)pyridylmethylthio]-pyrimidine
	Ex./Cpd #116	4-amino-6-methylthio-2-[2-(4-thiophenyl)pyridylmethylthio]-pyrimidine
	Ex./Cpd #117	4-amino-6-methylthio-2-[2-(3-methyl)pyridylmethylthio]-pyrimidine
5	Ex./Cpd #118	4-amino-6-methylthio-2-[2-(5-methyl)pyridylmethylthio]-pyrimidine
	Ex./Cpd #119	4-amino-6-methylthio-2-[2-(4-bromo)pyridylmethylthio]-pyrimidine
	Ex./Cpd #120	4-amino-6-methylthio-2-[2-(4-methoxy-6-methyl)-pyridylmethylthio]-pyrimidine
10	Ex./Cpd #121	4-amino-6-methylthio-2-[2-(4,6-dimethyl)pyridylmethylthio]-pyrimidine
	Ex./Cpd #122	4-amino-6-methylthio-2-[2-(4-ethyl)pyridylmethylthio]-pyrimidine
	Ex./Cpd #123	4-amino-6-methylthio-2-[2-(4-methoxy)pyridylmethylthio]-pyrimidine
	Ex./Cpd #124	4-amino-6-methylthio-2-[2-(4-(2-methylpropyl))pyridylmethylthio]-pyrimidine
15	Ex./Cpd #125	4-amino-6-methylthio-2-[2-(6-chloro-4-methyl)pyridylmethylthio]-pyrimidine
	Ex./Cpd #126	4-amino-6-methylthio-2-[2-(4-isopropoxy)pyridylmethylthio]-pyrimidine
20	Ex./Cpd #127	4-amino-6-methylthio-2-[2-(4,6-dimethyl)pyrimidinylmethylthio]-pyrimidine
	Ex./Cpd #128	4-amino-6-methylthio-2-[2-(4-cyano)pyridylmethylthio]-pyrimidine
	Ex./Cpd #130	4-amino-6-methylthio-2-[4-(6-methyl)pyrimidinylmethylthio]-pyrimidine
	Ex./Cpd #131	4-amino-6-methylthio-2-[2-(4-propyl)pyridylmethylthio]-pyrimidine
25	Ex./Cpd #132	4-amino-6-methylthio-2-[2-(4-isopropyl)pyridylmethylthio]-pyrimidine
	Ex./Cpd #133	4-amino-6-methylthio-2-[2-(5-phenyl)pyridylmethylthio]-pyrimidine
	Ex./Cpd #134	4-amino-6-methylthio-2-[2-(4-ethyl)pyridylmethylthio]-pyrimidine
30	Ex./Cpd #135	4-amino-6-methylthio-2-[2-(4-(α -hydroxy, α -methyl)ethyl)pyridylmethylthio]-pyrimidine
	Ex./Cpd # 137	4-amino-6-methylthio-2-[2-(4-cyclopropyl)pyridylmethylthio]-pyrimidine
	Ex./Cpd # 138	4-amino-6-methylthio-2-[2-(4-cyclopentyl)pyridylmethylthio]-pyrimidine
35	Ex./Cpd #140	4-amino-6-methylthio-2-[2-(4,5-dimethyl)pyridylmethylthio]-pyrimidine

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- Ex./Cpd #142 4-amino-6-methylthio-2-[4-(2,6-dimethyl)pyrimidinylmethylthio]-pyrimidine
- Ex./Cpd #143 4-amino-6-methylthio-2-[2-(4-pyrrolidino)pyridylmethylthio]-pyrimidine
- 5 Ex./Cpd #144 4-Amino-6-methylthio-2-[(5-chlorothiophen-2-ylmethyl)thio]pyrimidine
- Ex./Cpd #145 4-amino-6-methylthio-2-[2-(4-(2-butyl))pyridylmethylthio]-pyrimidine
- Ex./Cpd #146 4-amino-6-methylthio-2-[2-(4-dimethylamino)pyridylmethylthio]-pyrimidine
- 10 Ex./Cpd #147 2-[2-(4-amino-6-methylthio)pyrimidinylthiomethyl]-pyridine-1-oxide
- Ex./Cpd #148 4-Amino-6-methylthio-2-[(furan-3-ylmethyl)thio]pyrimidine
- Ex./Cpd #149 4-amino-6-methylthio-5-fluoro-2-[2-(4-chloro)pyridylmethylthio]pyrimidine
- Ex./Cpd #151 4-amino-6-methylthio-2-[2-(4-(3-pentyl))pyridylmethylthio]-pyrimidine
- 15 Ex./Cpd #152 4-amino-6-methylthio-2-[2-(4-acetyl)pyridylmethylthio]-pyrimidine
- Ex./Cpd #153 4-Amino-6-methylthio-2-[(benzofuran-2-ylmethyl)thio]pyrimidine
- Ex./Cpd #154 4-amino-6-methylthio-2-[2-(6-dimethylamino-4-methyl)pyridylmethylthio]-pyrimidine
- 20 Ex./Cpd #155 4-amino-6-methylthio-2-[(1H-inden-3-ylmethyl)thio]pyrimidine
- Ex./Cpd #156 4-amino-6-methylthio-2-[2-(4-carbomethoxy)pyridylmethylthio]-pyrimidine
- Ex./Cpd #157 4-Amino-6-methylthio-2-[(S)-(-)-perillyl]thio]pyrimidine
- Ex./Cpd #158 4-Amino-6-methylthio-2-[(benzothiophen-2-ylmethyl)thio]pyrimidine
- 25 Ex./Cpd #159 4-Amino-6-methylthio-2-[(2H-1-benzopyran-3-ylmethyl)thio]pyrimidine
- Ex./Cpd #163 4-amino-6-methylthio-2-[2-(4-carboxamido)-pyridylmethylthio]-pyrimidine
- Ex./Cpd #164 4-amino-6-methylthio-2-[2-(4-hydroxymethyl)-pyridylmethylthio]-pyrimidine
- 30 Ex./Cpd #165 4-amino-5-bromo-6-methylthio-2-[2-(4-methyl)pyridylmethylthio]-pyrimidine
- Ex./Cpd #166 4-amino-5-bromo-6-methylthio-2-[2-(4-isopropyl)-pyridylmethylthio]-pyrimidine
- 35 Ex./Cpd #167 4-amino-6-methylthio-2-(2,6-dichlorophenyl)methylthio-pyrimidine
- Ex./Cpd #168 4-Amino-6-methylthio-2-[(2,3-dihydrobenzofuran-5-ylmethyl)thio]

		pyrimidine
	Ex./Cpd #167	4-amino-6-methylthio-2-(2,6-dichlorophenyl)methylthio-pyrimidine
	Ex./Cpd #168	4-Amino-6-methylthio-2-[(2,3-dihydrobenzofuran-5-ylmethyl)thio]pyrimidine
5	Ex./Cpd #169	4-Amino-6-methylthio-2-[(5-phenylisoxazol-3-ylmethyl)thio]-pyrimidine
	Ex./Cpd #170	4-Amino-6-methylthio-2-[(2,3-dihydrobenzofuran-2-ylmethyl)thio]pyrimidine
	Ex./Cpd #171	4-Amino-6-methylthio-2-[(3,4-dihydro-1-naphthalen-2-yl)methyl]thio]-pyrimidine
10	Ex./Cpd# 172	4-Amino-6-methylthio-2-[(5-chloroimidazo[1,2-a]pyridin-2-yl)methyl]thio]-pyrimidine
	Ex./Cpd #173	4-Amino-6-methylthio-2-[(6-methylpyrazin-2-ylmethyl)thio]pyrimidine
15	Ex./Cpd #174	4-Amino-6-methylthio-2-[(5-methylisoxazol-3-ylmethyl)thio]pyrimidine
	Ex./Cpd #175	4-Amino-6-methylthio-2-[(5-methylpyrazin-2-ylmethyl)thio]pyrimidine
	Ex./Cpd #176	4-Amino-6-methylthio-2-[(1-methylimidazol-2-ylmethyl)thio]pyrimidine
20	Ex./Cpd #177	4-Amino-6-methylthio-2-[(3-methylpyrazin-2-ylmethyl)thio]pyrimidine
	Ex./Cpd #178	4-Amino-6-methylthio-2-[(quinolin-6-ylmethyl)thio]pyrimidine
	Ex./Cpd #179	4-Amino-6-methylthio-2-[(quinoxalin-2-ylmethyl)thio]pyrimidine
25	Ex./Cpd # 180	4-Amino-6-methylthio-2-[(quinolin-8-ylmethyl)thio]pyrimidine
	Ex./Cpd #181	4-Amino-6-methylthio-2-[(quinolin-4-ylmethyl)thio]pyrimidine
	Ex./Cpd #182	4-Amino-6-methylthio-2-[(isoquinolin-3-ylmethyl)thio]pyrimidine
	Ex./Cpd #183	4-Amino-6-methylthio-2-[(quinolin-5-ylmethyl)thio]pyrimidine
30	Ex./Cpd #184	4-Amino-6-methylthio-2-[(quinolin-7-ylmethyl)thio]pyrimidine
	Ex./Cpd #186	4-Amino-6-methylthio-2-[(piperon-5-ylmethyl)thio]pyrimidine
	Ex./Cpd #187	4-Amino-6-methylthio-2-[(3,4-dihydro-1-naphthalenyl)methyl]thio]pyrimidine
	Ex./Cpd #188	4-amino-6-methylthio-2[2-(5-carbomethoxy)pyridylmethylthio]pyrimidine
35	Ex./Cpd #189	4-amino-6-methylthio-2[2-(4-cyclohexyl)pyridylmethylthio]

		pyrimidine
	Ex./Cpd #191	4-chloro-5-fluoro-6-methylthio-2-[2-(4-chloro)pyridyl-methylthio]pyrimidine
	Ex./Cpd #192	4-amino-5-fluoro-6-methylthio-2-[2-(4-chloro)pyridyl-methylthio]pyrimidine
5		
	Ex./Cpd #193	(<i>E</i>)-4-[(4-Amino-6-methylthio-2-pyrimidinyl)thio]-2-butenic acid methyl ester
	Ex./Cpd #194	(<i>E</i>)- <i>N,N</i> -Diethyl-4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-2-butenamide
10	Ex./Cpd #195	(<i>E</i>)-4-methyl-1-[4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-1-oxo-2-butenyl]piperazine
	Ex./Cpd #196	(<i>E</i>)- <i>N</i> -ethyl-4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-2-butenamide
	Ex./Cpd #197	(<i>E</i>)-1-[4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-1-oxo-2-butenyl]piperidine
15		
	Ex./Cpd #198	(<i>E</i>)-4-[4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-1-oxo-2-butenyl]morpholine
	Ex./Cpd #199	(<i>E</i>)-1-[4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-1-oxo-2-butenyl]pyrrolidine
20	Ex./Cpd #200	(<i>E</i>)- <i>N</i> -methyl- <i>N</i> -phenyl-4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-2-butenamide
	Ex./Cpd #201	(<i>E</i>)- <i>N</i> -allyl- <i>N</i> -methyl-4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-2-butenamide
	Ex./Cpd #202	(<i>E</i>)- <i>N,N</i> -Dipropyl-4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-2-butenamide
25		
	Ex./Cpd #203	(<i>E</i>)- <i>N</i> -ethyl- <i>N</i> -methyl-4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-2-butenamide
	Ex./Cpd #204	(<i>E</i>)- <i>N,N</i> -Dimethyl-4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-2-butenamide
30	Ex./Cpd #207	(<i>E</i>)- <i>N,N</i> -Diethyl-4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-2-pentenamide
	Ex./Cpd #208	(<i>E</i>)-4-[(4-Amino-6-methylthio-2-pyrimidinyl)thio]-3-methyl-2-butenic acid methyl ester
	Ex./Cpd #209	(<i>E</i>)-4-[(4-Amino-6-methylthio-2-pyrimidinyl)thio]-3-methyl-2-pentenoic acid methyl ester
35		
	Ex./Cpd #210	4-Amino-6-methylthio-2-(1-(4-(1,1-dimethyl)ethyl)-2-

		pyridyl)ethyl)thio-pyrimidine
	Ex./Cpd #211	4-Amino-6-methylthio-2-(1-(2-pyridyl)ethyl)thio-pyrimidine
	Ex./Cpd #212	4-Amino-6-methylthio-2-(1-(2-pyridyl)-1-methylethyl)thio-pyrimidine
	Ex./Cpd #213	4-Amino-6-methylthio-2-(1-(2-(4-methyl)pyridyl)-1-methylethyl)thio-
5		pyrimidine
	Ex./Cpd #214	4-Amino-6-methylthio-2-(1-(4-cyano-2-pyridyl)ethyl)thio-pyrimidine
	Ex./Cpd #215	4-Amino-6-methylthio-2-(1-(4-methyl-2-pyridyl)ethyl)thio-
		pyrimidine hydrochloride
	Ex./Cpd #216	4-Amino-6-methylthio-2-(1-(4-ethyl-2-pyridyl)ethyl)thio-pyrimidine
10	Ex./Cpd #217	4-Amino-6-methylthio-2-(1-(4-methyl-2-pyridyl)-1-cyanomethyl)thio-
		pyrimidine
	Ex./Cpd #218	4-Amino-6-methylthio-2-(1-(4-methyl-2-pyridyl)propyl)thio-
		pyrimidine
	Ex./Cpd #219	4-Amino-6-methylthio-2-(1-(4-acetyl-2-pyridyl)ethyl)thio-pyrimidine
15	Ex./Cpd #220	4-Amino-6-methylthio-2-(1-(4-methyl-2-pyridyl)-1-carbomethoxy-
		methyl)thio-pyrimidine
	Ex./Cpd #221	4-Amino-6-methylthio-2-(1-(4-(1-methylethenyl)-2-pyridyl)ethyl)thio-
		pyrimidine
	Ex./Cpd #223	4-Amino-6-methylthio-2-(1-(4-(1-methylethyl)-2-pyridyl)ethyl)thio-
20		pyrimidine
	Ex./Cpd #224	4-Amino-6-methylthio-2-(1-(4-methyl-2-pyridyl)pentyl)thio-
		pyrimidine
	Ex./Cpd #225	4-Amino-5-bromo-6-methylthio-2-(1-(4-methylethyl)-2-
		pyridyl)ethyl)thio-pyrimidine
25	Ex./Cpd #226	4-Amino-6-methylthio-2-(1-(4-methyl-2-pyridyl)-1-cyclopropyl-
		methyl)thio-pyrimidine mesylate
	Ex./Cpd #227	4-Amino-6-methylthio-2-(1-(4-(4-morpholinyl)methyl-2-
		pyridyl)ethyl)thio-pyrimidine
	Ex./Cpd #228	4-Amino-6-methylthio-2-(1-(4-dimethylaminomethyl-2-
30		pyridyl)ethyl)thio-pyrimidine
	Ex./Cpd #229	4-Amino-6-methylthio-2-(1-(2-naphthalenyl)ethyl)thio-pyrimidine
	Ex./Cpd #230	4-Amino-6-methylthio-2-(1-(3-isoquinolyl)ethyl)thio-pyrimidine
	Ex./Cpd #231	4-Amino-5-bromo-6-methylthio-2-(1-(3-isoquinolyl)ethyl)thio-
		pyrimidine
35	Ex./Cpd #232	4-Amino-6-methylthio-2-(1-(1-isoquinolyl)ethyl)thio-pyrimidine
	Ex./Cpd #233	4-Amino-6-methylthio-2-(1-(3-(5,6,7,8-tetrahydro-

		isoquinolyl)ethylthio-pyrimidine
	Ex./Cpd #235	4-Amino-6-methylthio-2-(1-(1-(5,6,7,8-tetrahydroisoquinolyl))-ethylthio-pyrimidine
5	Ex./Cpd #236	4-Amino-5-bromo-6-methylthio-2-(1-(1-(5,6,7,8-tetrahydroisoquinolyl)ethylthio-pyrimidine
	Ex./Cpd #237	4-Amino-6-methylthio-2-(1-(7-chlorofuro[2,3-c]pyridine-5-yl)ethylthio-pyrimidine
	Ex./Cpd #238	4-Amino-6-methylthio-2-(1-(furo[2,3-c]pyridin-5-yl)ethylthio-pyrimidine
10	Ex./Cpd #240	4-Amino-6-methylthio-2-(1-(7-chloro-2-methylfuro[2,3-c]pyridine-5-yl)ethylthio-pyrimidine
	Ex./Cpd #242	4-Amino-6-methylthio-2-(1-(2-methylfuro[2,3-c]pyridine-5-yl)ethylthio-pyrimidine
	Ex./Cpd #244	4-Amino-6-methylthio-2-(1-(6-chloro-5-methoxy-4-vinyl-2-pyridyl)ethylthio-pyrimidine
15	Ex./Cpd #245	4-Amino-6-methylthio-2-(1-(4-ethyl-5-methoxy-2-pyridyl)ethylthio-pyrimidine
	Ex./Cpd #246	4-Amino-6-methylthio-2-(1-(3-methylfuro[2,3-c]pyridine-5-yl)ethylthio-pyrimidine
20	Ex./Cpd #247	4-Amino-6-methylthio-2-(1-(2,3-dihydrofuro[2,3-c]pyridine-5-yl)ethylthio-pyrimidine
	Ex./Cpd #248	4-Amino-6-methylthio-2-(1-(3,3-dimethyl-2,3-dihydrofuro[2,3-c]pyridine-5-yl)ethylthio-pyrimidine
	Ex./Cpd #249	4-Amino-6-methylthio-2-(1-(3-ethylfuro[2,3-c]pyridine-5-yl)ethylthio-pyrimidine
25	Ex./Cpd #250	4-Amino-6-methylthio-2-(1-(7-chloro-3,3-dimethyl-2,3-dihydrofuro[2,3-c]pyridine-5-yl)ethylthio-pyrimidine
	Ex./Cpd #251	4-Amino-6-methylthio-2-(1-(7-chloro-3-ethylfuro-[2,3-c]pyridine-5-yl)ethylthio-pyrimidine
30	Ex./Cpd #252	4-Amino-6-methylthio-2-(1-(3-(1-methylethyl)furo[2,3-c]-pyridin-5-yl)ethylthio-pyrimidine
	Ex./Cpd #253	4-amino-6-methylthio-2-(1-(4-cylcopentyl)-2-pyridyl)-ethylthio-pyrimidine
	Ex./Cpd #255	4-amino-6-methylthio-2-(1-(4-cylcopropyl)-2-pyridyl)-ethylthio-pyrimidine
35	Ex./Cpd #256	4-amino-6-methylthio-2-(1-(4-(1-methylpropyl)-2-pyridyl)-

		ethyl)thio-pyrimidine
	Ex./Cpd #257	4-amino-6-methylthio-2-(1-(4-cylcohexyl)-2-pyridyl)-ethyl)thio-pyrimidine
	Ex./Cpd #258	4-amino-6-methylthio-2-(1-(4-(1-pyrryl))-2-pyridyl)-ethyl)thio-pyrimidine
5		
	Ex./Cpd #259	4-amino-6-methylthio-2-(1-(4-dimethylamino)-2-pyridyl)-ethyl)thio-pyrimidine
	Ex./Cpd #260	4-amino-6-methylthio-2-(1-(5-(1-methylethyl)-3-pyridyl)-ethyl)thio-pyrimidine
10	Ex./Cpd #261	4-amino-6-methylthio-2-(1-(4-(1-ethylpropyl)-2-pyridyl)-ethyl)thio-pyrimidine
	Ex./Cpd #262	4-amino-6-methylthio-2-(1-(4-methyl-6-(1-pyrryl))-2-pyridyl)-ethyl)thio-pyrimidine
	Ex./Cpd #263	4-amino-6-methylthio-2-(1-(4-(2-propyloxy))-2-pyridyl)-ethyl)thio-pyrimidine
15		
	Ex./Cpd #282	4-amino-6-methylthio-2-(1-(3-chloro-[2,3-c]pyridine-5-yl)ethyl)thio-pyrimidine
	Ex./Cpd #283	4-Amino-6-methylthio-2-(1-(3,7-dichlorofuro[2,3-c]pyridine-5-yl)ethyl)thio-pyrimidine
20	Ex./Cpd #284	4-Amino-6-methylthio-2-(1-(3-bromofuro[2,3-c]pyridine-5-yl)ethyl)thio-pyrimidine
	Ex./Cpd #285	4-Amino-6-methylthio-2-(1-(3-bromo-7-chlorofuro[2,3-c]pyridine-5-yl)ethyl)thio-pyrimidine
	Ex./Cpd #286	4-Amino-6-methylthio-2-(1-(7-chloro-3-methylfuro[2,3-c]pyridine-5-yl)ethyl)thio-pyrimidine
25		
	Ex./Cpd #289	(R)-(+)-4-Amino-6-methylthio-2-(1-(3-methylfuro[2,3-c]pyridine-5-yl)ethyl)thio-pyrimidine
	Ex./Cpd #290	(S)-(-)-4-Amino-6-methylthio-2-(1-(3-methylfuro[2,3-c]pyridine-5-yl)ethyl)thio-pyrimidine, mp 80-82°C
30	Ex./Cpd #291	R-(+)-4-Amino-6-methylthio-2-(1-(4-ethyl-2-pyridyl)ethyl)thio-pyrimidine
	Ex./Cpd #292	(-)-4-Amino-6-methylthio-2-(1-(4-ethyl-2-pyridyl)ethyl)thio-pyrimidine
	Ex./Cpd #293	4-amino-6-methylthio-2-(1-(7-chloro-3-trifluoromethyl)-furo[2,3-c]pyridin-5-yl)ethylthio-pyrimidine
35		
	Ex./Cpd #294	4-Amino-6-methylthio-2-(1-(3-trifluoromethyl)-furo[2,3-c]pyridin-5-

- yl)ethylthio)-pyrimidine
- Ex./Cpd #300 (R)-(+)-4-Amino-6-methylthio-2-(1-(furo[2,3-c]pyridin-5-yl)ethylthio)-pyrimidine
- Ex./Cpd #301 (S)-(-)-4-Amino-6-methylthio-2-(1-(furo[2,3-c]pyridin-5-yl)ethylthio)-pyrimidine mesylate salt
- 5 Ex./Cpd #302 (S)-(-)-4-Amino-6-methylthio-2-(1-(3-methylfuro[2,3-c]pyridin-5-yl)ethylthio)-pyrimidine, esylate salt
- Ex./Cpd #303 4-amino-6-methylthio-2-(((5-benzyloxy-6-chloro)-2-pyridyl)-ethyl)thio-pyrimidine
- 10 Ex./Cpd #304 4-amino-6-methylthio-2-(furo[2,3-b]pyridin-5-yl-methylthio)-pyrimidine

Following the above procedures and making non-critical variations, the following compounds are prepared:

- 15 4-Amino-6-methylthio-2-(1-(3-trifluoromethylfuro[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(7-chloro-3-trifluoromethylfuro[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 20 4-Amino-6-methylthio-2-(1-(3-fluorofuro[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-((2,2,2-trifluoro)ethyl)furo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 25 4-Amino-6-methylthio-2-(1-(3-((1-trifluoromethyl-2,2,2-trifluoro)ethyl)furo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 30 4-Amino-6-methylthio-2-(1-(3-cyanofuro[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-carbomethoxyfuro[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 35 4-Amino-6-methylthio-2-(1-(3-aminocarbonylfuro[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

- 4-Amino-6-methylthio-2-(1-(3-(N,N-dimethylaminocarbonyl)furo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 5 4-Amino-6-methylthio-2-(1-(3-(methylsulfonylamino)furo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-(methylcarboxyamino)furo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 10 4-Amino-6-methylthio-2-(1-(3-phenylfuro[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-(tert-butyl)furo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-cyclopropylfuro[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 15 4-Amino-6-methylthio-2-(1-(3-fluorothieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-((2,2,2-trifluoro)ethyl)thieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 20 4-Amino-6-methylthio-2-(1-(3-((1-trifluoromethyl-2,2,2-trifluoro)ethyl)thieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-cyanothieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 25 4-Amino-6-methylthio-2-(1-(3-carbomethoxythieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-aminocarbonylthieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 30 4-Amino-6-methylthio-2-(1-(3-(N,N-dimethylaminocarbonyl)thieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 35 4-Amino-6-methylthio-2-(1-(3-(methylsulfonylamino)thieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

- 4-Amino-6-methylthio-2-(1-(3-(methylcarboxyamino)thieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 5 4-Amino-6-methylthio-2-(1-(3-phenylthieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-(tert-butyl)thieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 10 4-Amino-6-methylthio-2-(1-(3-cyclopropylthieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-fluoro-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 15 4-Amino-6-methylthio-2-(1-(3-((2,2,2-trifluoro)ethyl)-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-((1-trifluoromethyl-2,2,2-trifluoro)ethyl)-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 20 4-Amino-6-methylthio-2-(1-(3-cyano-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-carbomethoxy-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 25 4-Amino-6-methylthio-2-(1-(3-aminocarbonyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 30 4-Amino-6-methylthio-2-(1-(3-(N,N-dimethylaminocarbonyl)-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-(methylsulfonylamino)-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 35 4-Amino-6-methylthio-2-(1-(3-(methylcarboxyamino)-1H-pyrrolo[2,3-c]pyridin-5-

yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(3-phenyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

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4-Amino-6-methylthio-2-(1-(3-(tert-butyl)-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

10 4-Amino-6-methylthio-2-(1-(3-cyclopropyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(3-fluoro-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

15 4-Amino-6-methylthio-2-(1-(3-((2,2,2-trifluoro)ethyl)-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(3-((1-trifluoromethyl-2,2,2-trifluoro)ethyl)-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

20

4-Amino-6-methylthio-2-(1-(3-cyano-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

25 4-Amino-6-methylthio-2-(1-(3-carbomethoxy-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(3-aminocarbonyl-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

30 4-Amino-6-methylthio-2-(1-(3-(N,N-dimethylaminocarbonyl)-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(3-(methylsulfonylamino)-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

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4-Amino-6-methylthio-2-(1-(3-(methylcarboxyamino)-1-methyl-1H-pyrrolo[2,3-

c[pyridin-5-yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(3-phenyl-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

5

4-Amino-6-methylthio-2-(1-(3-(tert-butyl)-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(3-cyclopropyl-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

10

4-Amino-6-methylthio-2-(1-(7-chlorothieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(thieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

15

4-Amino-6-methylthio-2-(1-(7-chloro-2-methylthieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(2-methylthieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

20

4-Amino-6-methylthio-2-(1-(3-methylthieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine

4-Amino-6-methylthio-2-(1-(2,3-dihydrothieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

25

4-Amino-6-methylthio-2-(1-(3,3-dimethyl-2,3-dihydrothieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(3-ethylthieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

30

4-Amino-6-methylthio-2-(1-(7-chloro-3,3-dimethyl-2,3-dihydrothieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(7-chloro-3-ethylthieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

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- 4-Amino-6-methylthio-2-(1-(3-(1-methylethyl)thieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(7-chloro-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-
5 pyrimidine,
- 4-Amino-6-methylthio-2-(1-(1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(7-chloro-2-methyl-1H-pyrrolo[2,3-c]pyridin-5-
10 yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(2-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 15 4-Amino-6-methylthio-2-(1-(3-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(2,3-dihydro-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
20 4-Amino-6-methylthio-2-(1-(3,3-dimethyl-2,3-dihydro-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-ethyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-
25 pyrimidine,
- 4-Amino-6-methylthio-2-(1-(7-chloro-3,3-dimethyl-2,3-dihydro-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 30 4-Amino-6-methylthio-2-(1-(7-chloro-3-ethyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-(1-methylethyl)-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
35 4-Amino-6-methylthio-2-(1-(7-chloro-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-

yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

5

4-Amino-6-methylthio-2-(1-(7-chloro-2-methyl-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(2-methyl-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

10

4-Amino-6-methylthio-2-(1-(3-methyl-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

15 4-Amino-6-methylthio-2-(1-(2,3-dihydro-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(3,3-dimethyl-2,3-dihydro-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

20

4-Amino-6-methylthio-2-(1-(3-ethyl-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(7-chloro-3,3-dimethyl-2,3-dihydro-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

25

4-Amino-6-methylthio-2-(1-(7-chloro-3-ethyl-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

30 4-Amino-6-methylthio-2-(1-(3-(1-methylethyl)-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(3-chlorothieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

35 4-Amino-6-methylthio-2-(1-(3,7-dichlorothieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

- 4-Amino-6-methylthio-2-(1-(3-bromothieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-bromo-7-chlorothieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 5 4-Amino-6-methylthio-2-(1-(7-chloro-3-methylthieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 10 4-Amino-6-methylthio-2-(1-(3-chloro-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3,7-dichloro-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 15 4-Amino-6-methylthio-2-(1-(3-bromo-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-bromo-7-chloro-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 20 4-Amino-6-methylthio-2-(1-(7-chloro-3-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 25 4-Amino-6-methylthio-2-(1-(3-chloro-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3,7-dichloro-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 30 4-Amino-6-methylthio-2-(1-(3-bromo-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 4-Amino-6-methylthio-2-(1-(3-bromo-7-chloro-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,
- 35

4-Amino-6-methylthio-2-(1-(7-chloro-3-methyl-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

5 4-Amino-6-methylthio-2-(1-(3-trifluoromethylthieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(7-chloro-3-trifluoromethylthieno[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

10 4-Amino-6-methylthio-2-(1-(3-trifluoromethyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

4-Amino-6-methylthio-2-(1-(7-chloro-3-trifluoromethyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

15

4-Amino-6-methylthio-2-(1-(3-trifluoromethyl-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine,

20 4-Amino-6-methylthio-2-(1-(7-chloro-3-trifluoromethyl-1-methyl-1H-pyrrolo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine.

CHART A

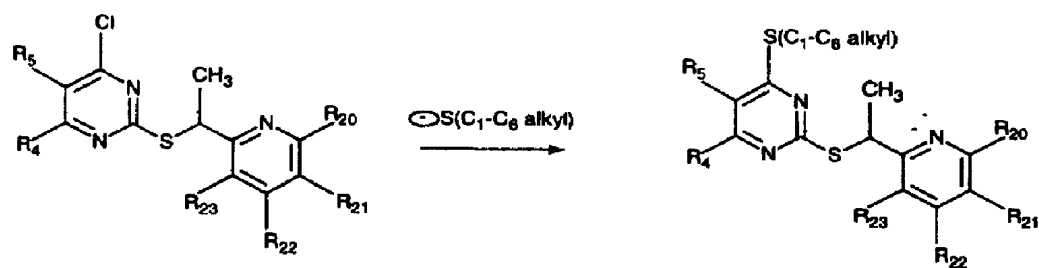
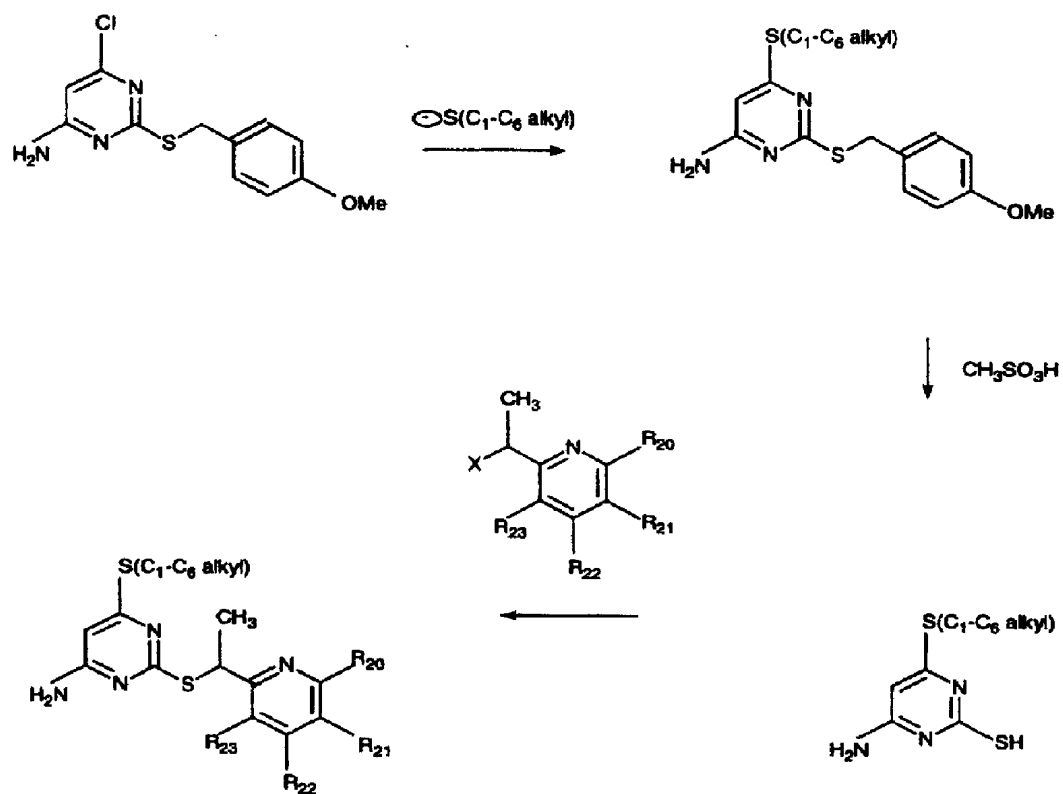
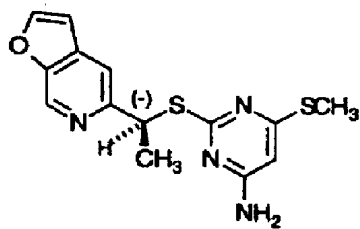


CHART B

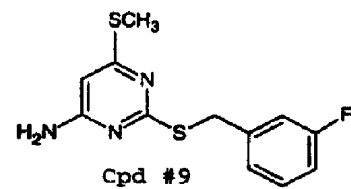
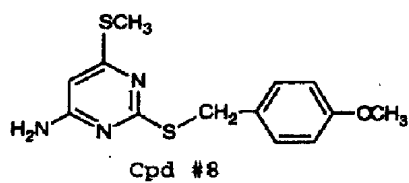
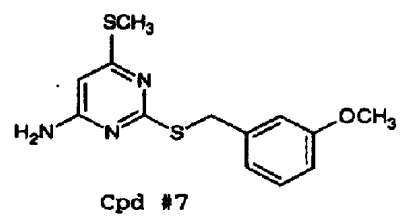
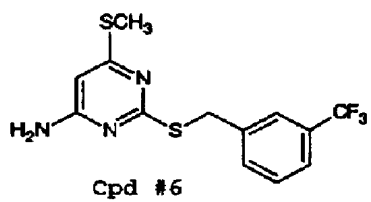
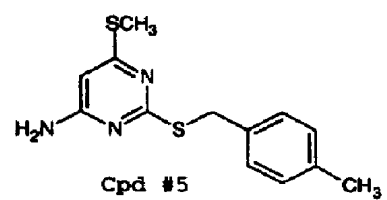
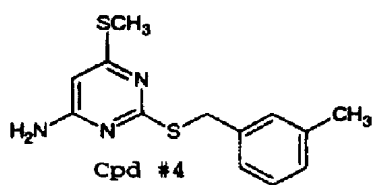
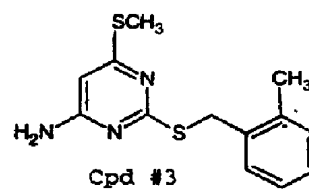
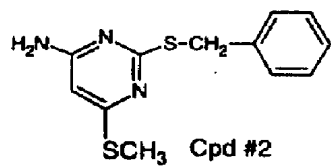


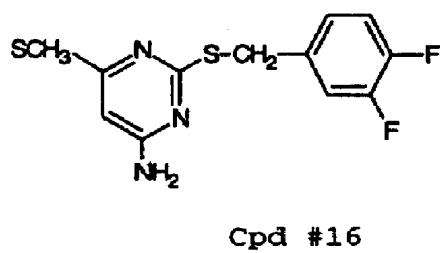
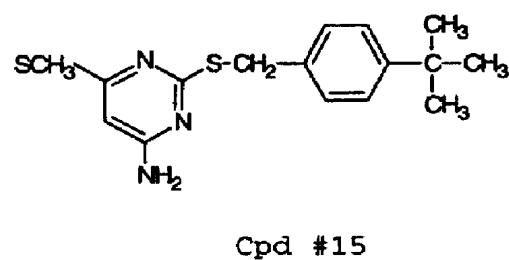
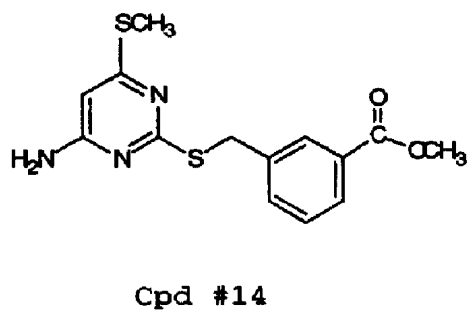
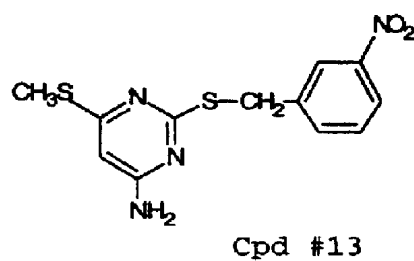
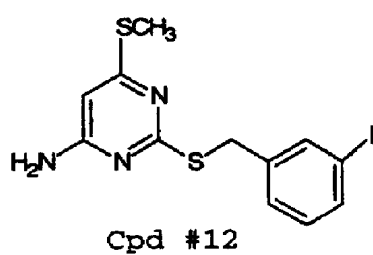
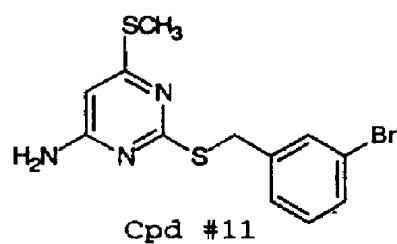
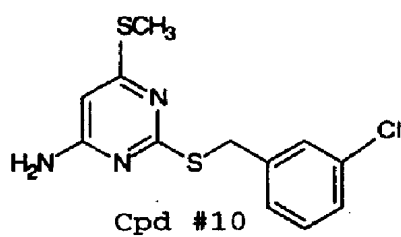
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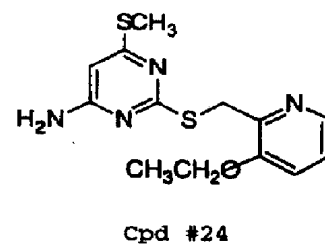
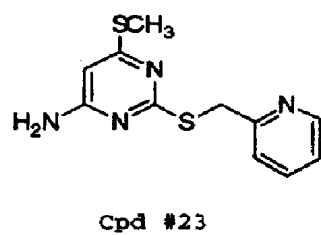
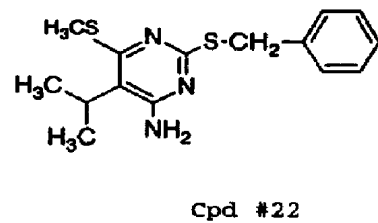
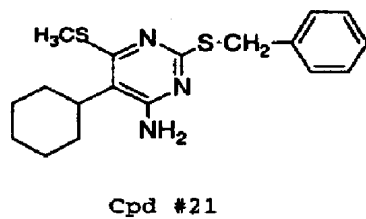
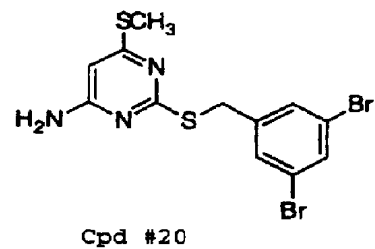
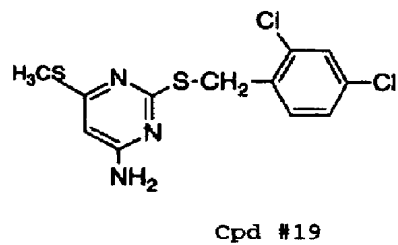
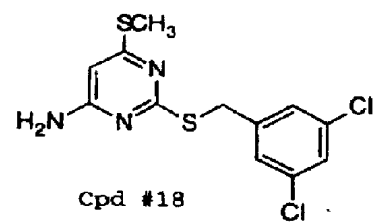
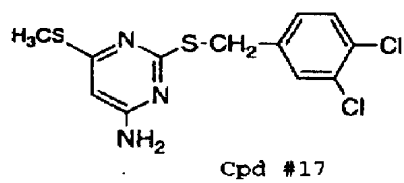


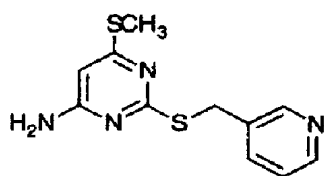
(S)-(-)enantiomer

Cpd #1

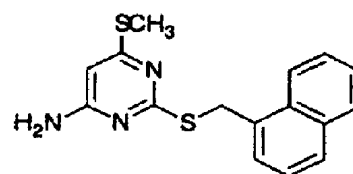




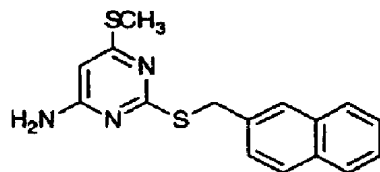




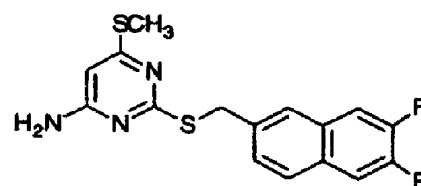
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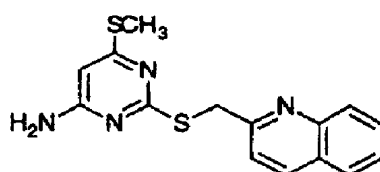
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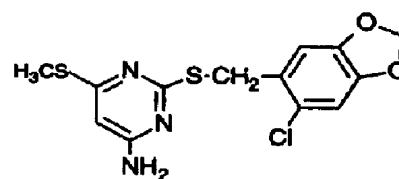
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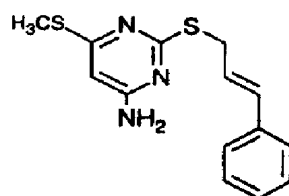
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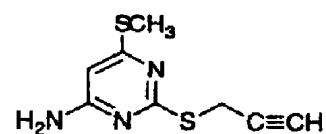
Cpd #29



Cpd #30



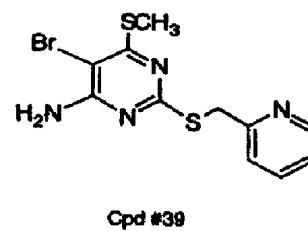
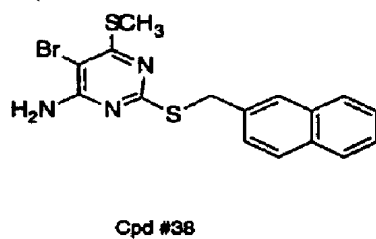
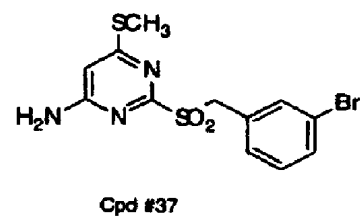
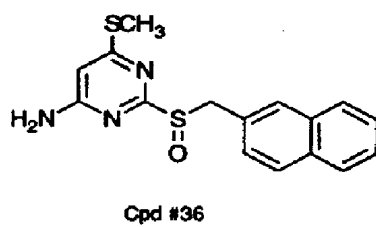
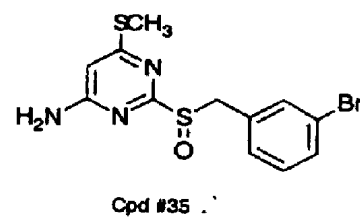
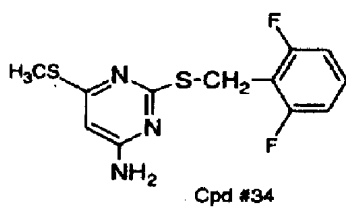
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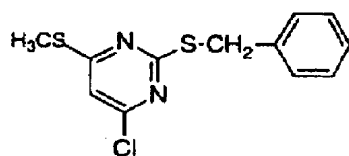


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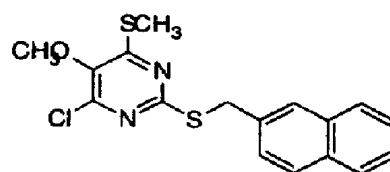
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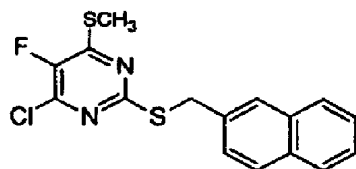




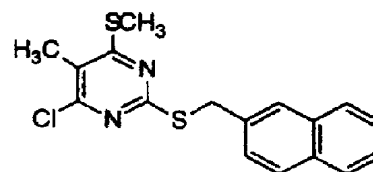
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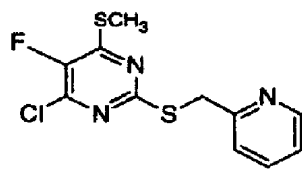
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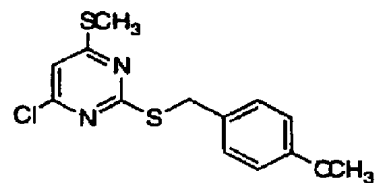
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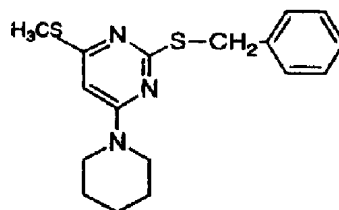
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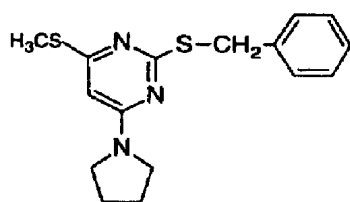
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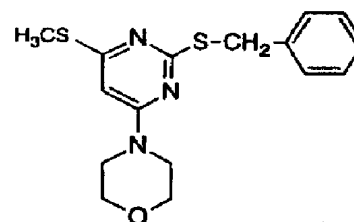
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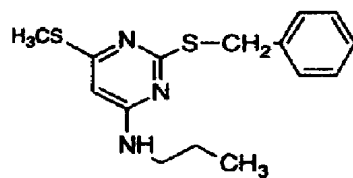
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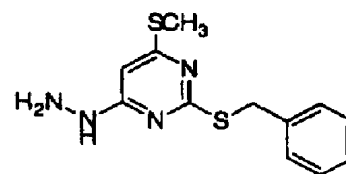
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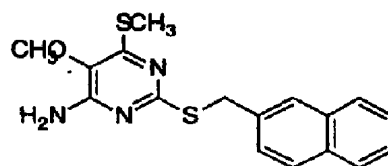
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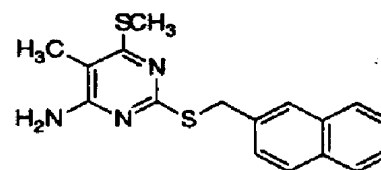
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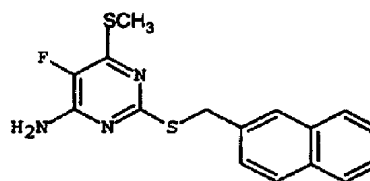
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Cpd #89



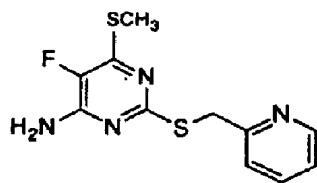
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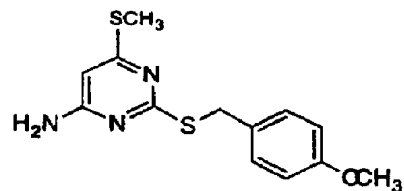
Cpd #91

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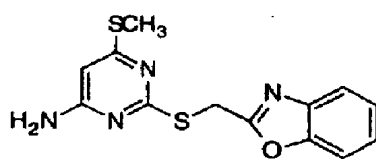
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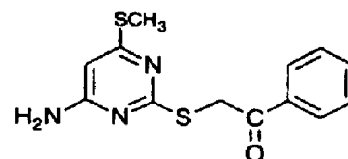
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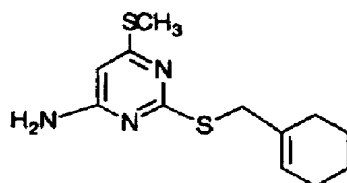
PCT/US98/18507



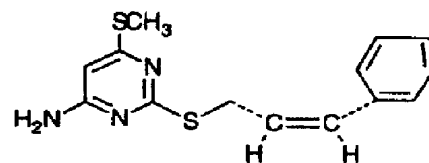
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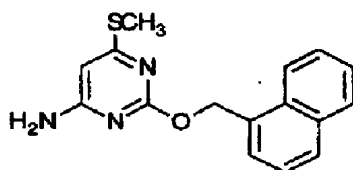


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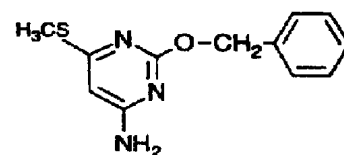


cis isomer

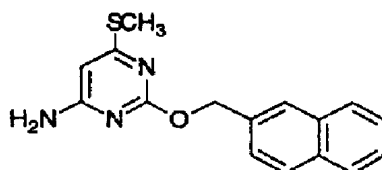
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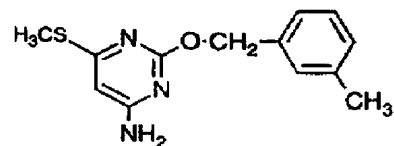
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Cpd #104



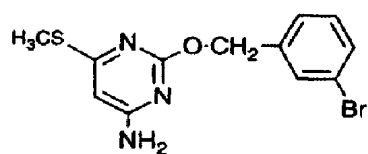
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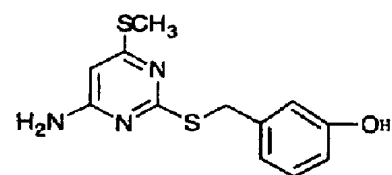
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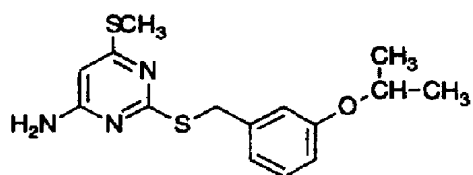
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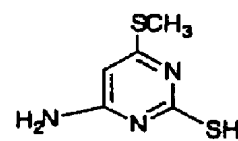
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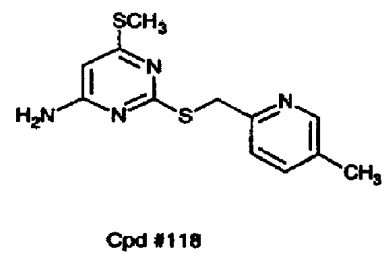
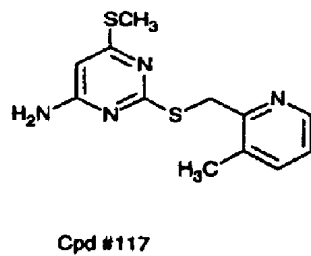
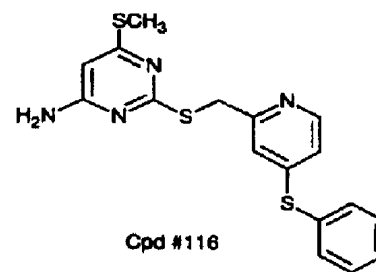
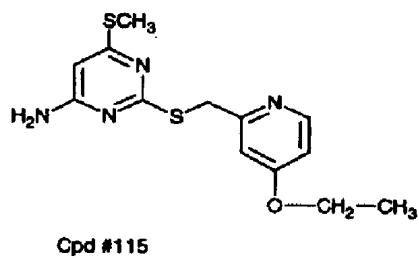
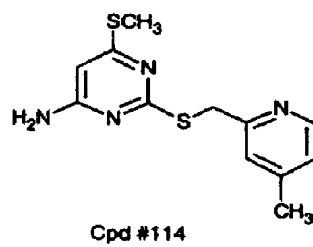
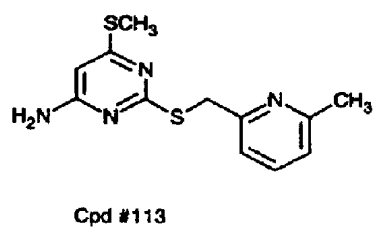
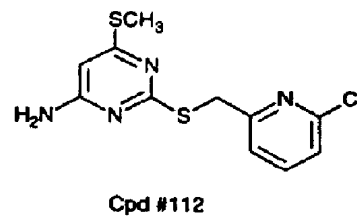
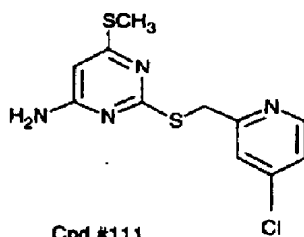
Cpd #108



Cpd #109

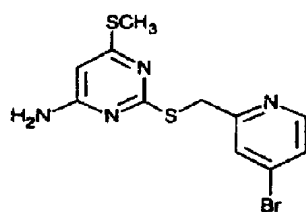


Cpd #110

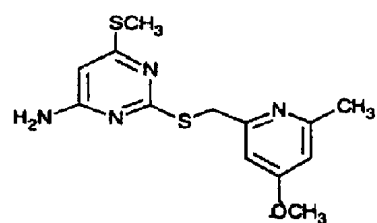


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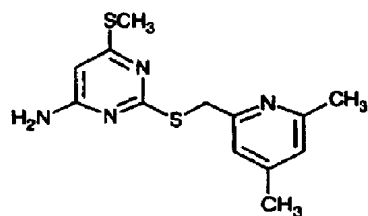
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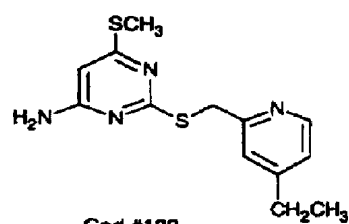
Cpd #119



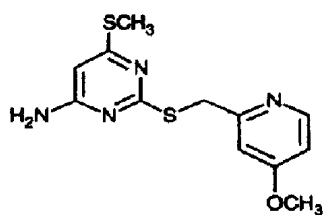
Cpd #120



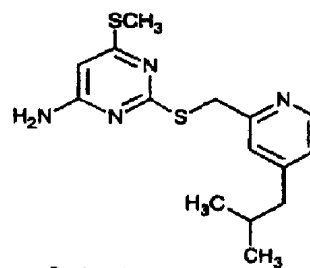
Cpd #121



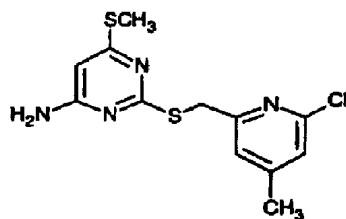
Cpd #122



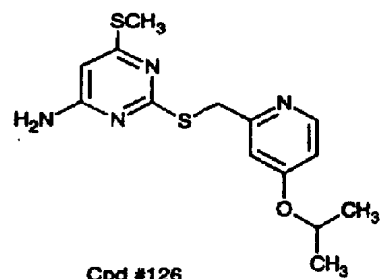
Cpd #123



Cpd #124



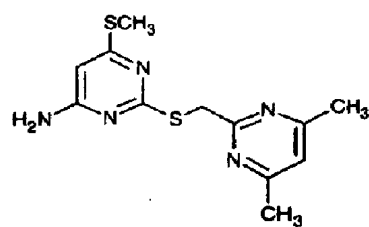
Cpd #125



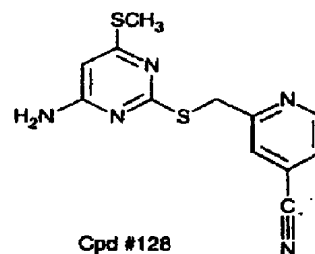
Cpd #126

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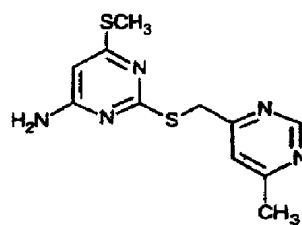
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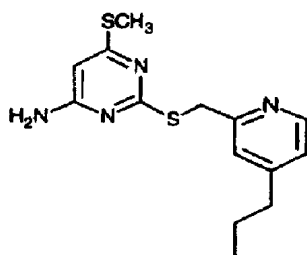
Cpd #127



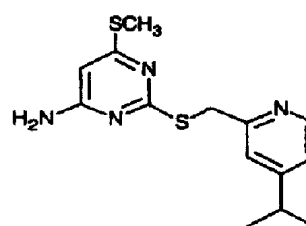
Cpd #128



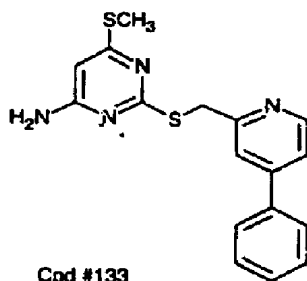
Cpd #130



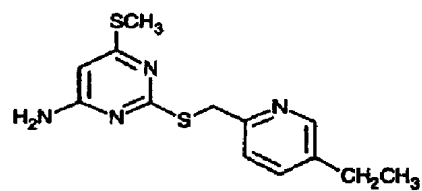
Cpd #131



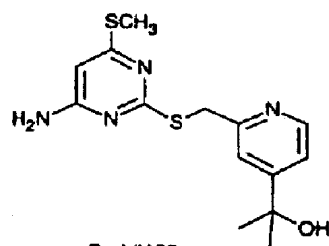
Cpd #132



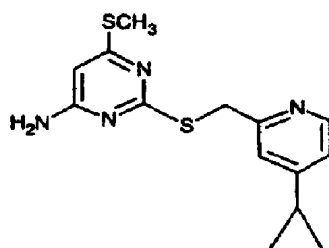
Cpd #133



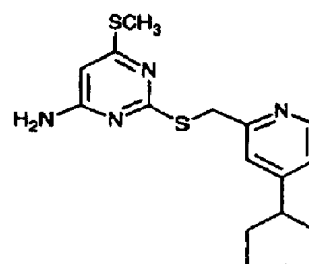
Cpd #134



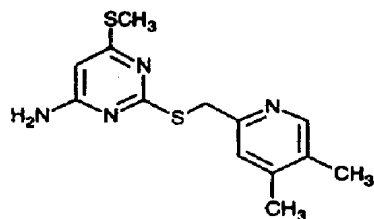
Cpd #135



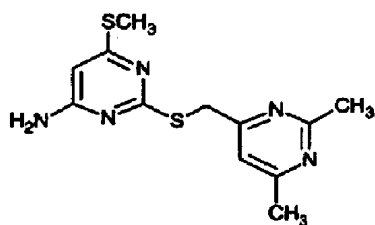
Cpd #137



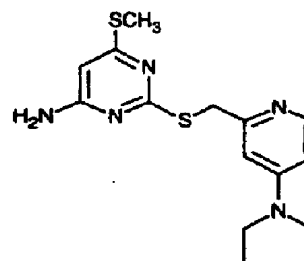
Cpd #138



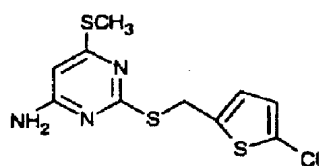
Cpd #140



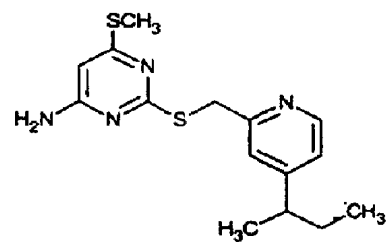
Cpd #142



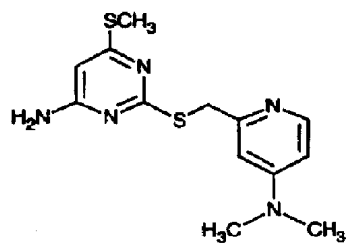
Cpd #143



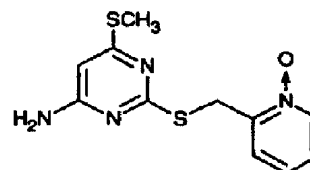
Cpd #144



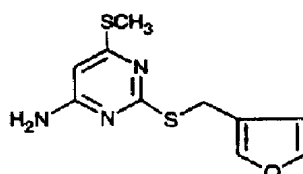
Cpd #145



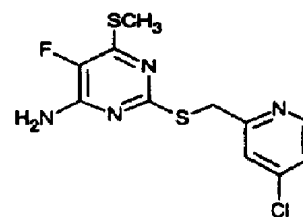
Cpd #146



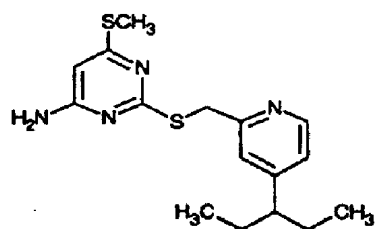
Cpd #147



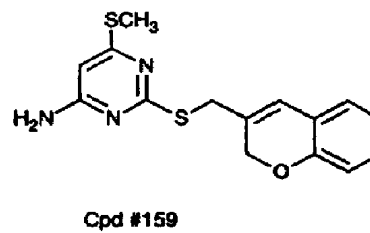
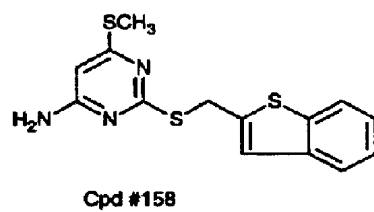
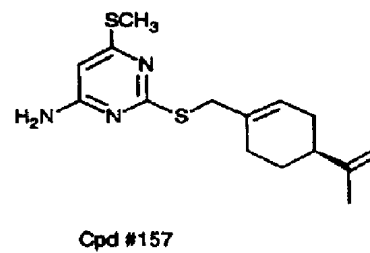
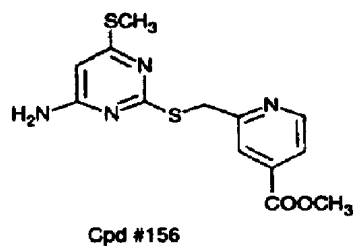
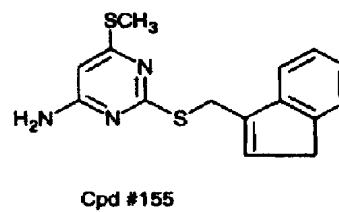
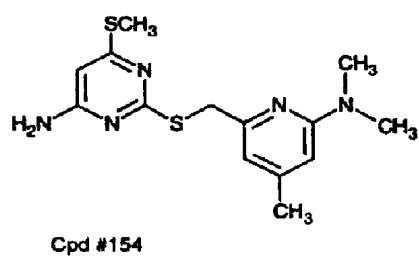
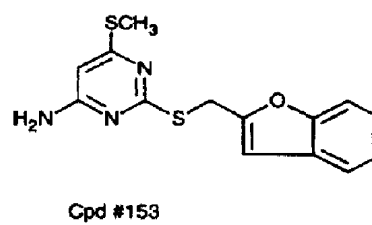
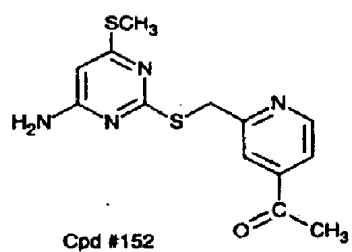
Cpd #148

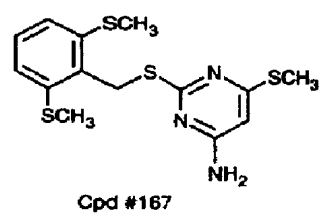
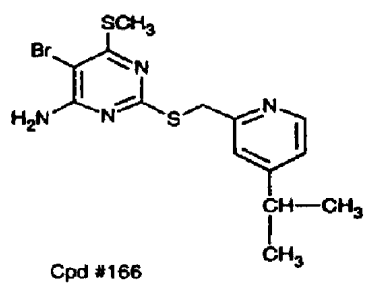
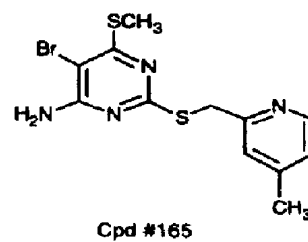
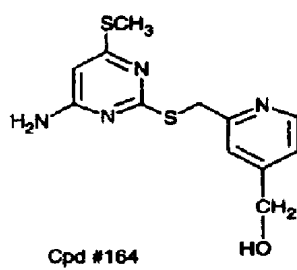
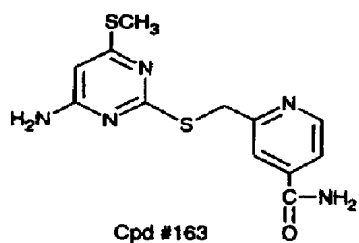


Cpd #149



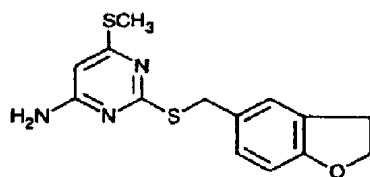
Cpd #151



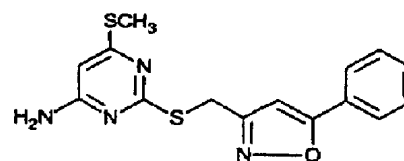


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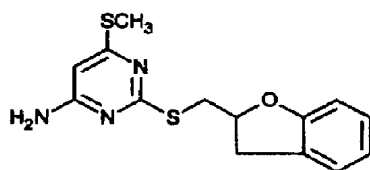
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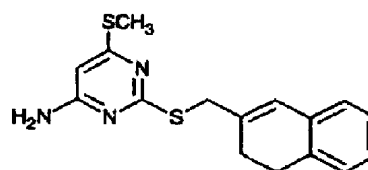
Cpd #168



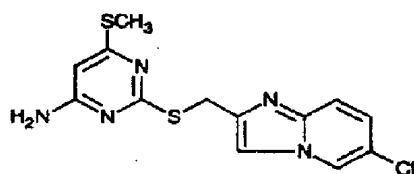
Cpd #169



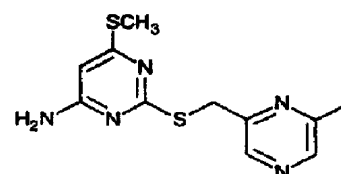
Cpd #170



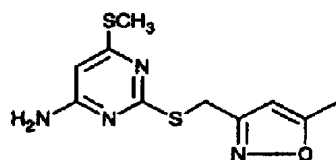
Cpd #171



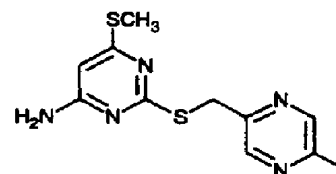
Cpd #172



Cpd #173



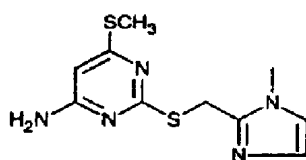
Cpd #174



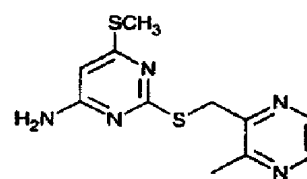
Cpd #175

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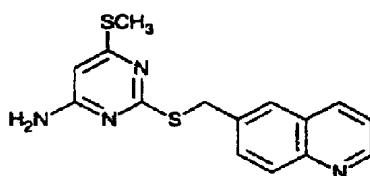
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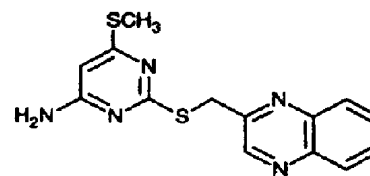
Cpd #176



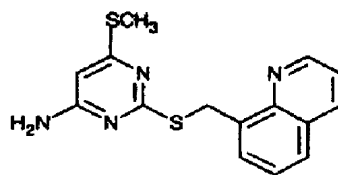
Cpd #177



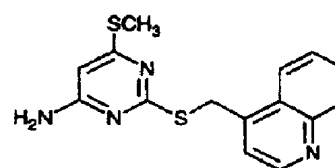
Cpd #178



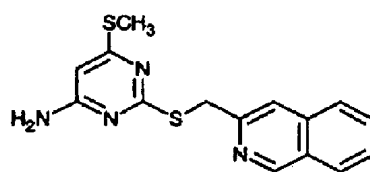
Cpd #179



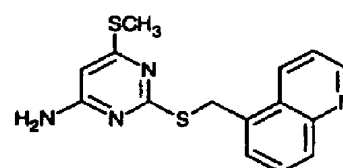
Cpd #180



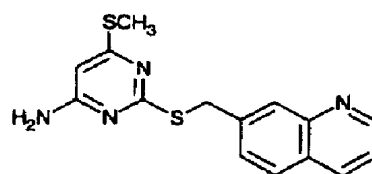
Cpd #181



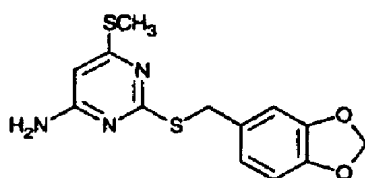
Cpd #182



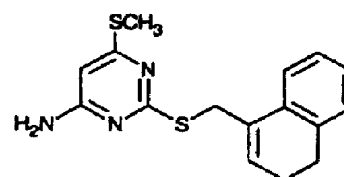
Cpd #183



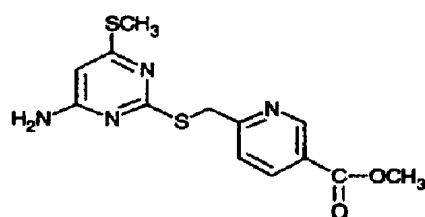
Cpd #184



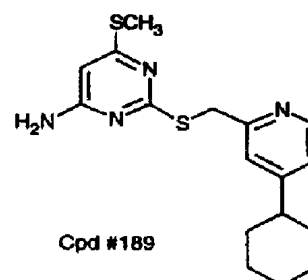
Cpd #186



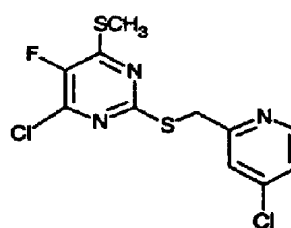
Cpd #187



Cpd #188



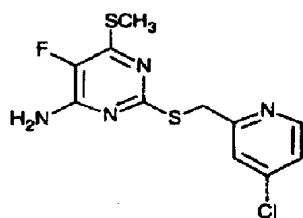
Cpd #189



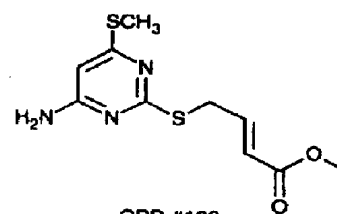
Cpd #191

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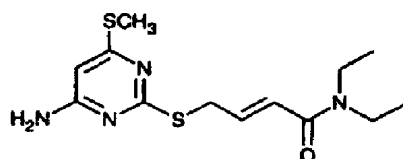
PCT/US98/18507



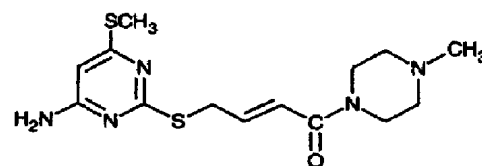
Cpd #192



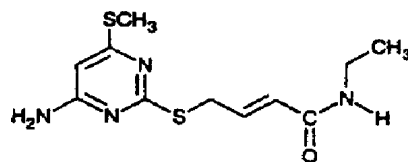
CPD #193



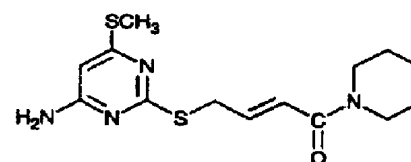
Cpd #194



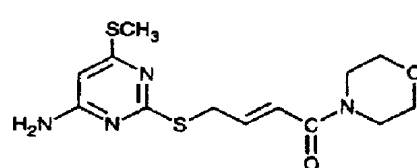
Cpd #195



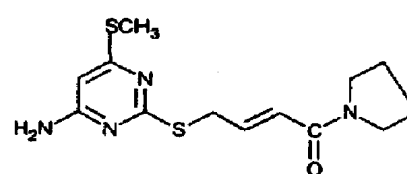
Cpd #196



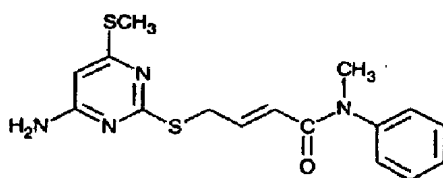
Cpd #197



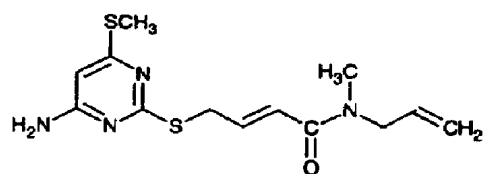
Cpd #198



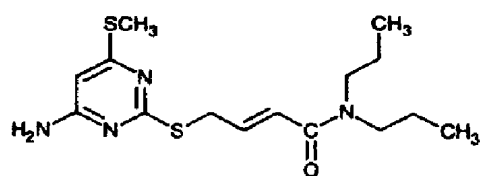
Cpd 199



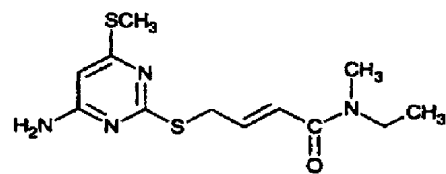
Cpd #200



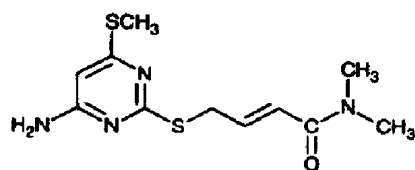
Cpd #201



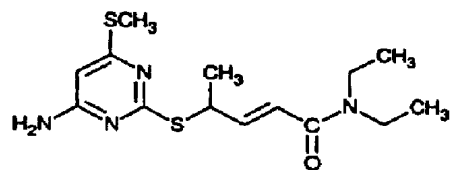
Cpd #202



Cpd #203



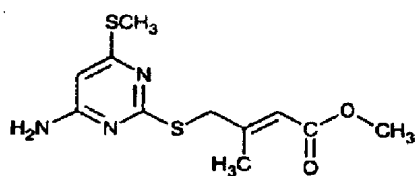
Cpd #204



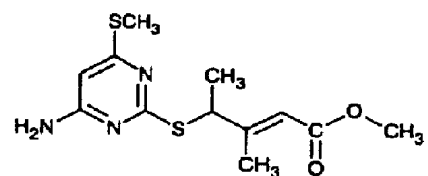
Cpd #207

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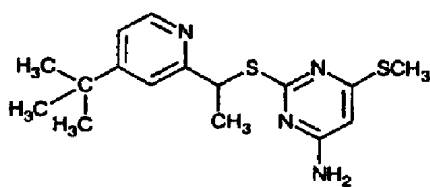
PCT/US98/18507



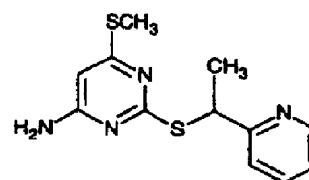
Cpd #208



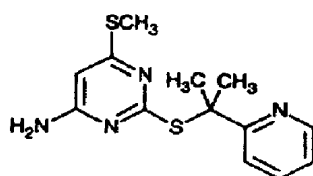
Cpd #209



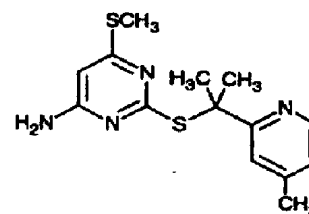
Cpd #210



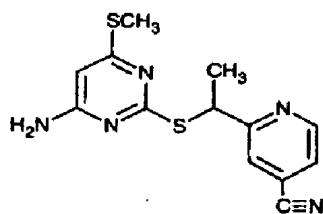
Cpd #211



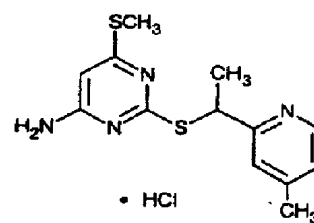
Cpd #212



Cpd #213

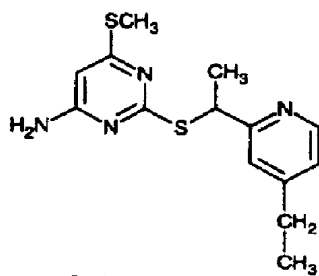


Cpd #214

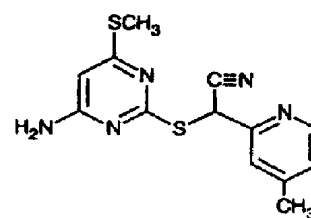


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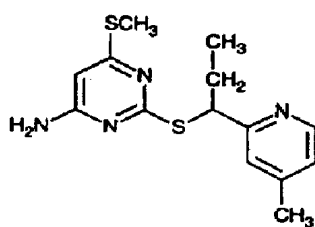
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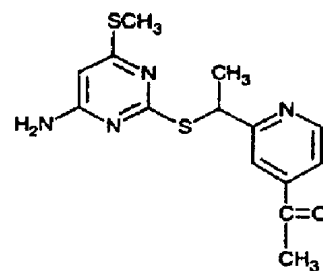
Cpd #216



Cpd #217



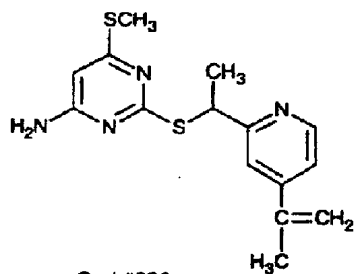
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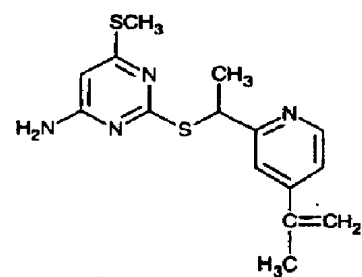
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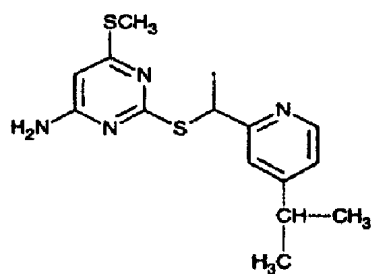
PCT/US98/18507



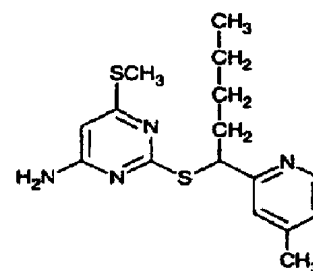
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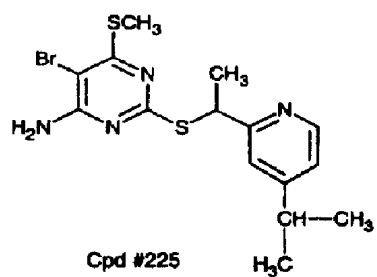
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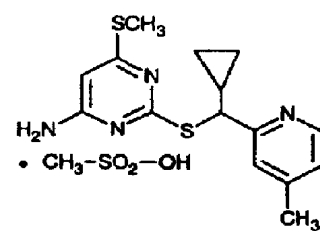
Cpd #223



Cpd #224



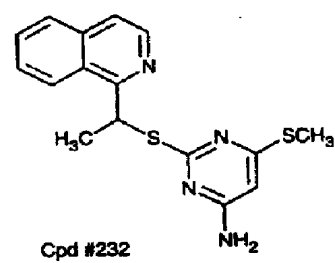
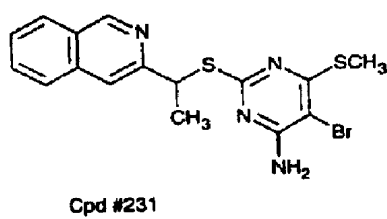
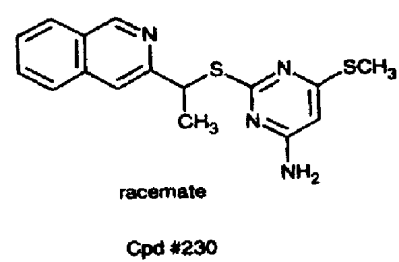
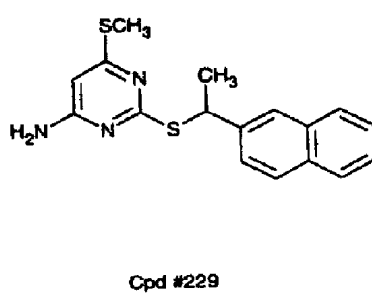
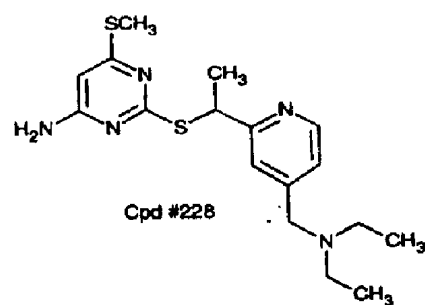
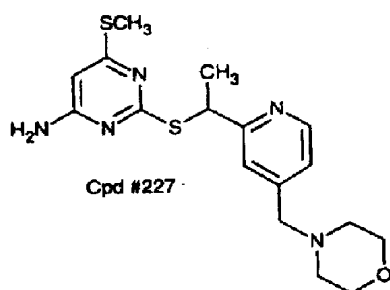
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Cpd #226

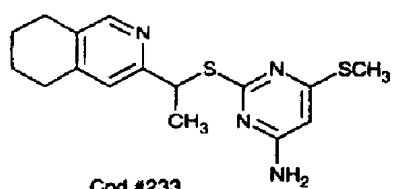
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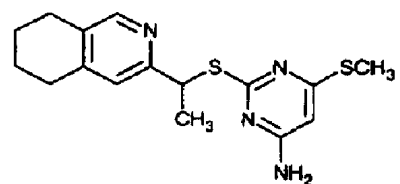


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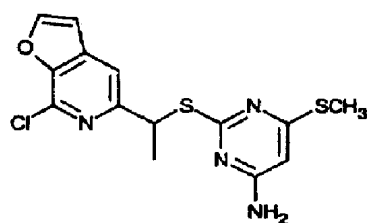
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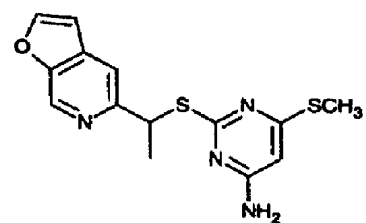
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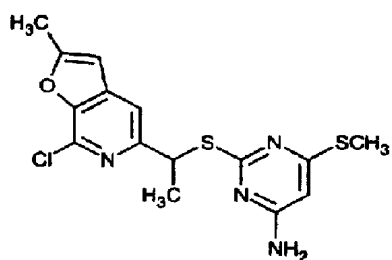
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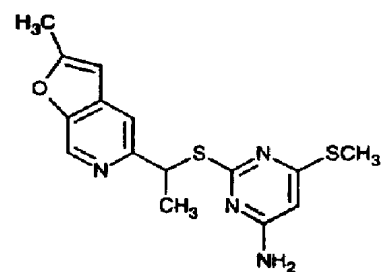
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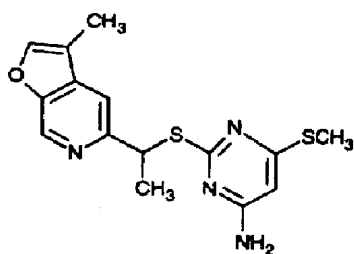
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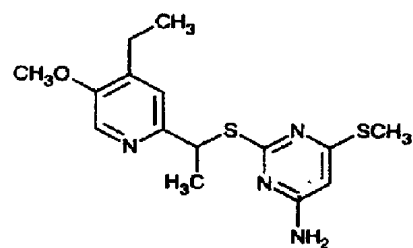
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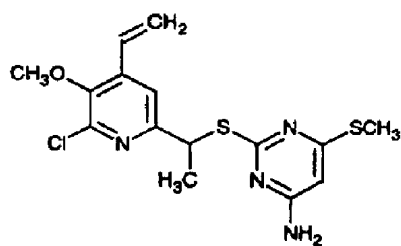
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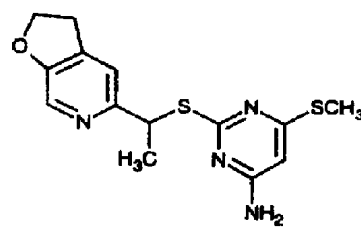
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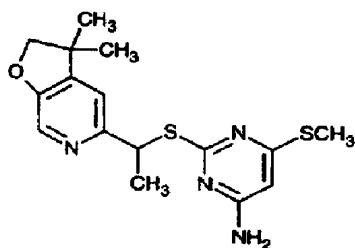
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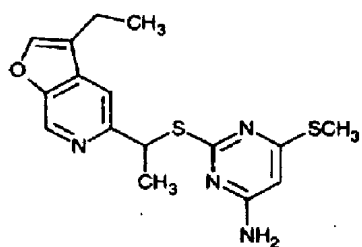
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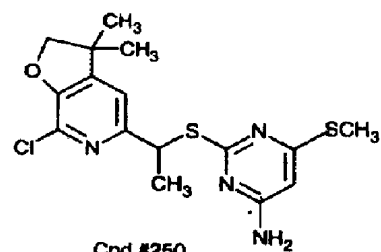
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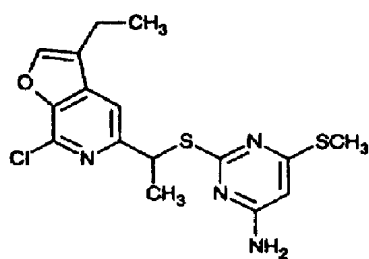
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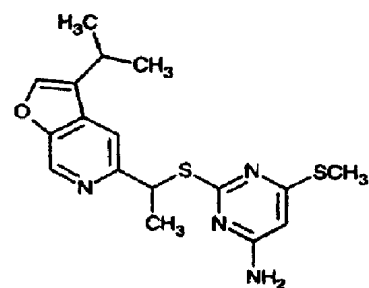
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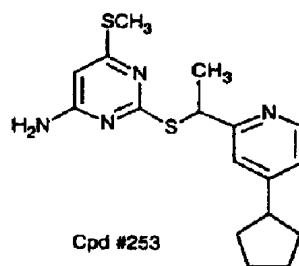
Cpd #250



Cpd #251



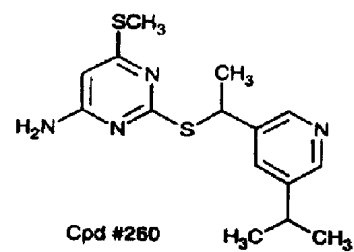
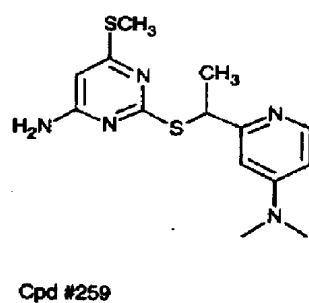
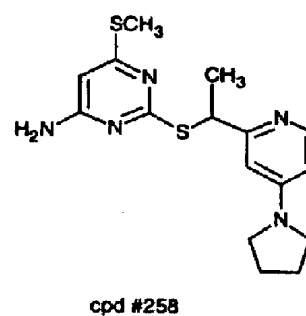
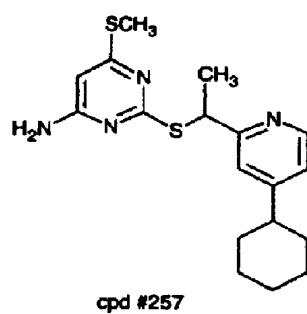
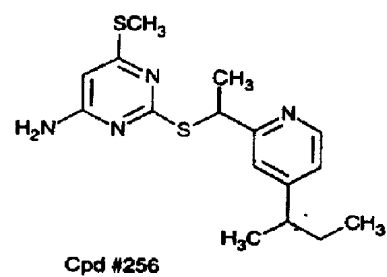
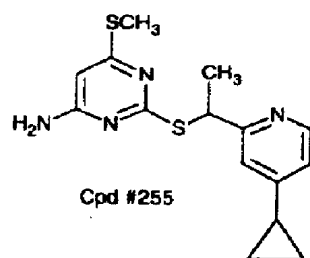
Cpd #252



Cpd #253

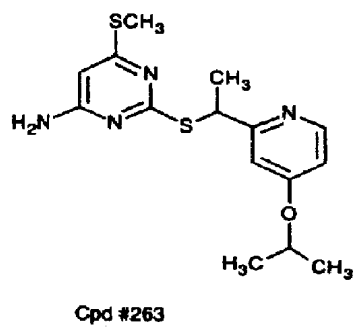
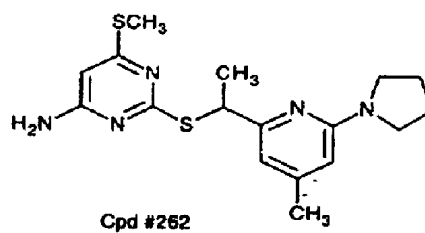
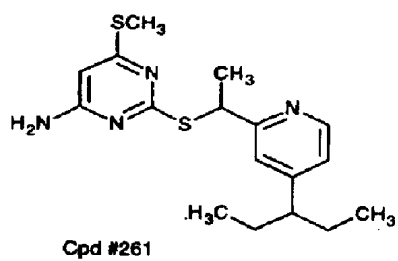
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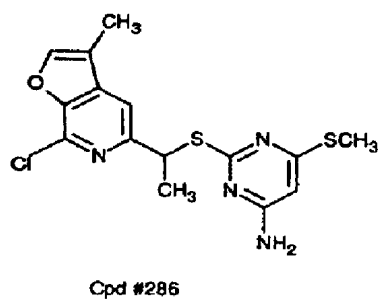
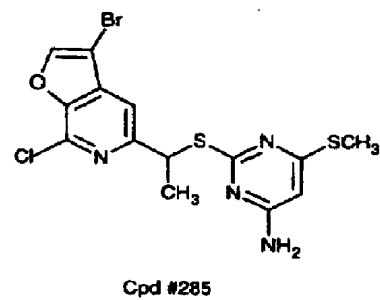
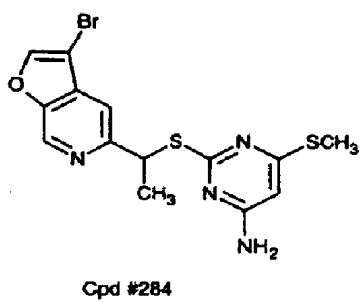
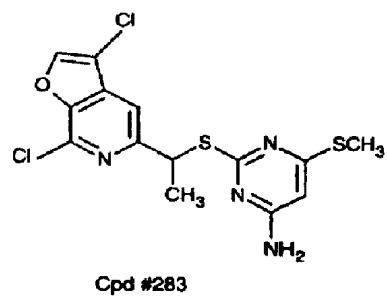
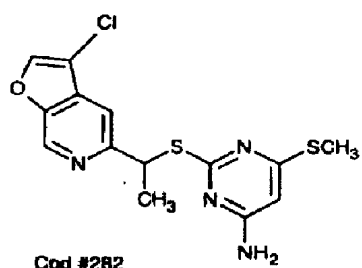
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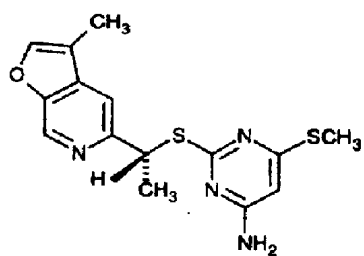
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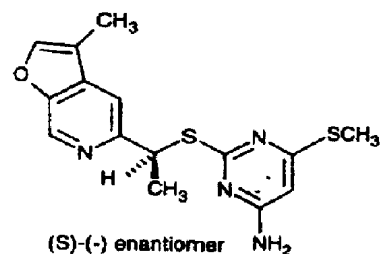
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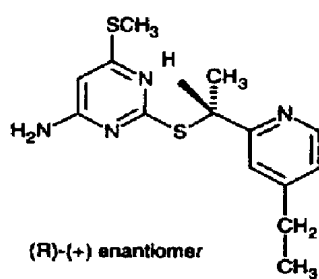
(R)-(+)-enantiomer

Cpd #289



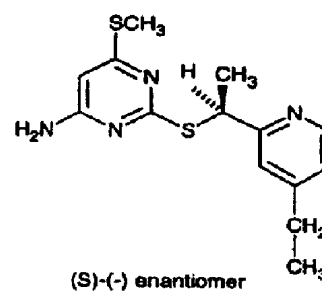
(S)-(-)-enantiomer

Cpd #290



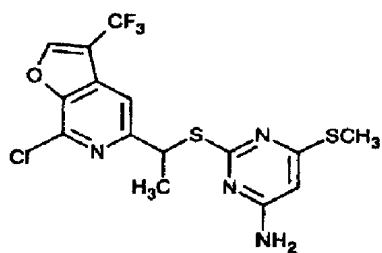
(R)-(+)-enantiomer

Cpd #291



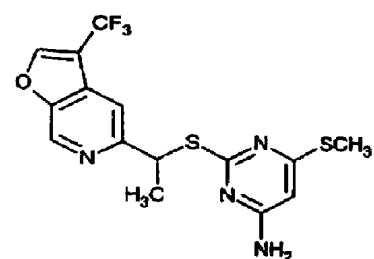
(S)-(-)-enantiomer

Cpd #292



racemate

Cpd #293 .

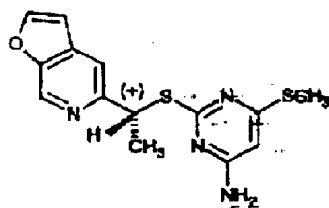


racemate

Cpd #294

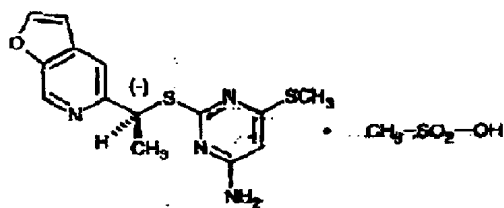
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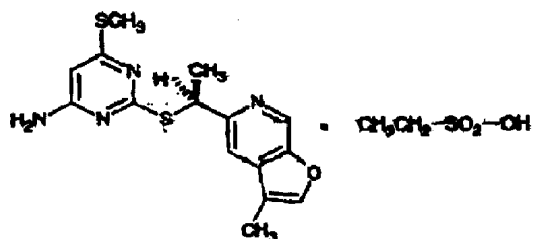
(R)-(+)-enantiomer

Cpd #300



(S)-(-)-enantiomer

Cpd #301

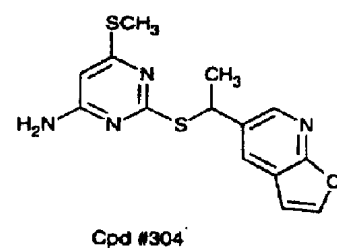
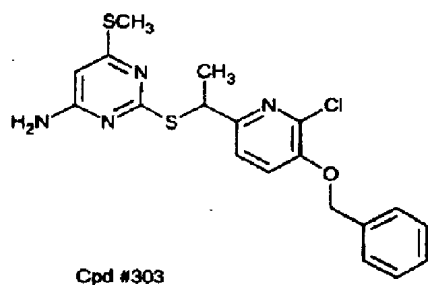


(S)-(-)-ENANTIOMER

Cpd #302

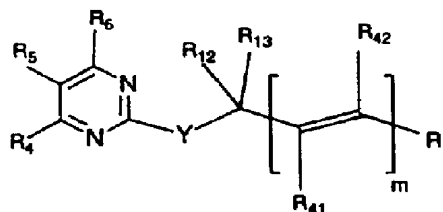
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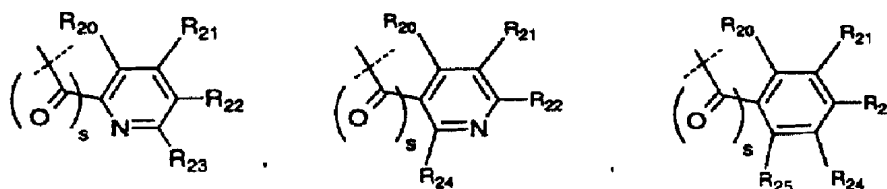
CLAIMS

1. A compound of Formula I



where m is 0 or 1;

R^1 is selected from the group consisting of $-C\equiv CH$, $-CO_2R_{53}$, $-CONR_{54}R_{55}$,



where s is 0 or 1 and R_{20} , R_{21} , R_{22} , R_{23} , R_{24} , and R_{25} are the same or different and are selected from $-H$, C_1 - C_6 alkyl, C_1 - C_6 alkenyl, C_1 - C_6 alkoxy, C_1 - C_6 alkylthio, $-C_3$ - C_8 cycloalkyl, $-CF_3$, $-NO_2$, $-halo$, $-OH$, $-CN$, phenyl, phenylthio, $-styryl$, $-CO_2(R_{31})$, $-CON(R_{31})(R_{32})$, $-CO(R_{31})$, $-(CH_2)_n-N(R_{31})(R_{32})$, $-C(OH)(R_{31})(R_{33})$, $-(CH_2)_n-N(R_{31})(CO(R_{33}))$, $(CH_2)_n-N(R_{31})(SO_2(R_{33}))$, or where R_{20} and R_{21} , or R_{21} and R_{22} , or R_{22} and R_{23} are taken together to form a five or six-membered saturated or unsaturated ring containing 0 or 1 oxygen, nitrogen or sulfur, where the unsaturated ring may be optionally substituted with 1, 2 or 3, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, $-OH$, $-CH_2OH$, $-(CH_2)_n-N(R_{31})(R_{32})$, $-C_3$ - C_8 cycloalkyl, $-CF_3$, $-halo$, $-CO_2(R_{31})$, $-CON(R_{31})(R_{32})$, $-CO(R_{31})$, $-(CH_2)_n-N(R_{31})(CO(R_{33}))$, $-(CH_2)_n-N(R_{31})(SO_2(R_{33}))$, $-CN$, $-CH_2CF_3$ or $-CH(CF_3)_2$, or phenyl, and the saturated ring may be optionally substituted with 1, 2 or 3, $-C_1$ - C_6

alkyl, $-C_1-C_6$ alkoxy, $-OH$, $-CH_2OH$ or $-(CH_2)_n-N(R_{31})(R_{32})$ or one oxo ($=O$);

where n is 0-3 and R_{31} , R_{32} , and R_{33} are the same or different and are selected from

- 5 $-H$,
 C_1-C_6 alkyl,
 phenyl optionally substituted with 1, 2, or 3 $-halo$, C_1-C_6 alkyl,
 C_1-C_6 alkoxy, $-CF_3$, $-OH$ or $-CN$,
 or where R_{31} and R_{32} taken together with the attached nitrogen to form a
- 10 ring selected from $-pyrrolidinyl$, $-piperidinyl$, $-4-morpholinyl$, $-4-thiomorpholinyl$, $-4-piperazinyl$, $-4-(1-C_1-C_6alkyl)piperazinyl$,
 or a member selected from the group consisting of:
 1-cyclohexenyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 2-imidazolyl,
 4-imidazolyl, 2-benzothiazolyl, 2-benzoxazolyl, 2-benzimidazolyl, 2-oxazolyl,
 15 4-oxazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 5-methyl-3-isoxazolyl, 5-phenyl-3-isoxazolyl, 4-thiazolyl, 3-methyl-2-pyrazinyl, 5-methyl-2-pyrazinyl, 6-methyl-2-pyrazinyl, 5-chloro-2-thienyl, 3-furyl, benzofuran-2-yl, benzothien-2-yl, 2*H*-1-benzopyran-3-yl, 2,3-dihydrobenzopyran-5-yl, 1-methylimidazol-2-yl, quinoxalin-2-yl, piperon-5-yl, 4,7-dichlorobenzoxazol-2-yl, 4,6-dimethylpyrimidin-2-yl, 4-methylpyrimidin-2-yl, 2,4-dimethylpyrimidin-6-yl, 2-methylpyrimidin-4-yl, 4-methylpyrimidin-6-yl, 6-chloropiperon-5-yl, 5-chloroimidazo[1,2-*a*]pyridin-2-yl, 1-*H*-inden-3-yl, 1-*H*-2-methyl-inden-2-yl, 3,4-dihydronaphth-1-yl, *S*-4-isopropenylcyclohexen-1-yl or 4-dihydronaphth-2-yl;
 where R_{53} is selected from the group consisting of $-H$, C_1-C_6alkyl , $C_3-C_6cycloalkyl$, phenyl (optionally substituted with 1, 2, or 3 $-halo$, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-CF_3$, $-OH$, $-CN$), or a five or six-membered unsaturated ring containing 0 or 1 oxygen, nitrogen or sulfur, where the unsaturated ring may be optionally substituted with $-H$, C_1-C_6 alkyl,
- 25 C_1-C_6 alkoxy, $-OH$, $-CH_2OH$, or $-(CH_2)_n-N(R_{31})(R_{32})$;
 where R_{54} and R_{55} being the same or different are selected from $-H$, C_1-C_6 alkyl, allyl, or phenyl (optionally substituted with 1, 2, or 3 $-halo$, C_1-C_6 alkyl, C_1-C_6 alkoxy or $-CF_3$), or taken together with the attached nitrogen to form a ring selected from $-pyrrolidinyl$, $-piperidinyl$, $-4-morpholinyl$, $-4-thiomorpholinyl$, $-4-piperazinyl$, $-4-(1-C_1-C_6alkyl)piperazinyl$;
- 30 R_{41} and R_{42} , being the same or different, are selected from the group
- 35

consisting of -H and C₁-C₄ alkyl;

R₁₂ is selected from the group consisting of -H, C₁-C₆ alkyl, -C₃-C₆ cycloalkyl, -CN, -C(O)NH₂, -C(O)N(C₁-C₆alkyl)(C₁-C₆alkyl), -CO₂H, -CO₂(C₁-C₆alkyl), -CH₂OH, -CH₂NH₂ or -CF₃;

5 R₁₃ is selected from the group consisting of -H, C₁-C₆ alkyl or -CF₃;

Y is selected from -S-, -S(O)-, -S(O)₂, or -O-;

R₄ is selected from the group consisting of -H, -OH, halo or -NR₁₅R₁₆ where R₁₅ is -H and R₁₆ is -H, C₁-C₆ alkyl, -NH₂ or R₁₅ and R₁₆ taken together with the -N form 1-pyrrolidino, 4-morpholino or 1-piperidino;

10 R₅ is selected from the group consisting of -H, -C₂H₄OH, -C₂H₄-O-TBDMS, halo, -C₃-C₆ cycloalkyl, C₁-C₄ alkyl or C₁-C₃ alkoxy;

or R₄ and R₅ are taken together to form a five or six-membered saturated or unsaturated ring which together with the pyrimidine ring form the group consisting of 7H-pyrrolo[2,3-d]pyrimidine, 5,6-dihydro-7H-pyrrolo[2,3-d]pyrimidine, furo[2,3-
15 d]pyrimidine, 5,6-dihydro-furo[2,3-d]pyrimidine, thieno[2,3-d]pyrimidine, 5,6-dihydro-thieno[2,3-d]pyrimidine, 1H-pyrazolo[3,4-d]pyrimidine, 1H-purine, pyrimido[4,5-d]pyrimidine, pteridine, pyrido[2,3-d]pyrimidine, or quinazoline, where the unsaturated ring may be optionally substituted with 1, 2 or 3, C₁-C₆ alkyl, C₁-C₆ alkoxy, -OH, -CH₂OH, or -(CH₂)_n-N(R₃₁)(R₃₂), -C₃-C₈ cycloalkyl, -CF₃, -halo, -
20 CO₂(R₃₁), -CON(R₃₁)(R₃₂), -CO(R₃₁), -(CH₂)_n-N(R₃₁)(CO(R₃₃)), -(CH₂)_n-N(R₃₁)(SO₂(R₃₃)), and the saturated ring may be optionally substituted with 1, 2 or 3, -C₁-C₆ alkyl, -C₁-C₆ alkoxy, -OH, -CH₂OH, or -(CH₂)_n-N(R₃₁)(R₃₂) or one oxo (=O); and

R₆ is -S-C₁₋₆ alkyl; or

pharmaceutically acceptable salts, hydrates, N-oxides and solvates thereof;

25

2. A compound according to Claim 1 where m is 0, s is 0 and Y is -S.

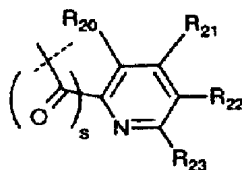
3. A compound according to Claim 2 where R₁₂ is CH₃ and R₁₃ is -H.

30

4. A compound according to Claim 3 where R₄ is NH₂, R₅ is -H, and R₆ is -SCH₃.

5. A compound according to Claim 3 where R₁ is

35



5

6. A compound according to Claim 5 wherein R_4 is NH_2 , R_5 is $-\text{H}$, and R_6 is $-\text{SCH}_3$.

7. A compound according to Claim 3 wherein R_1 is a five or six membered
- 10 saturated or unsaturated ring selected from the group consisting of 3-isoquinoliny, 1-isoquinoliny, 2-quinoliny, 3-quinoliny, 3-(5,6,7,8-tetrahydro)-isoquinoliny, 1-(5,6,7,8-tetrahydro)-isoquinoliny, 2-(5,6,7,8-tetrahydro)-quinoliny, 3-(5,6,7,8-tetrahydro)-quinoliny, 3-(5,6-dihydro)-2H-2-pyrindiny, 1-(5,6-dihydro)-2H-2-pyrindiny, 2-(5,6-dihydro)-1H-1-pyrindiny, 3-(5,6-dihydro)-1H-1-pyrindiny, 5-
- 15 furo[2,3-c]pyridiny, 6-furo[3,2-c]pyridiny, 4-furo[3,2-c]pyridiny, 7-furo[2,3-c]pyridiny, 6-furo[2,3-b]pyridiny, 5-furo[3,2-b]pyridiny, 5-(2,3-dihydro)-furo[2,3-c]pyridiny, 6-(2,3-dihydro)-furo[3,2-c]pyridiny, 4-(2,3-dihydro)-furo[3,2-c]pyridiny, 7-(2,3-dihydro)-furo[2,3-c]pyridiny, 6-(2,3-dihydro)-furo[2,3-b]pyridiny, 5-(2,3-dihydro)-furo[3,2-b]pyridiny, 6-(1,3-dihydro)-furo[3,4-c]pyridiny, 4-(1,3-dihydro)-
- 20 furo[3,4-c]pyridiny, 2-(5,7-dihydro)-furo[3,4-b]pyridiny, 6-(3,4-dihydro)-2H-pyrano[2,3-c]pyridiny, 6-(3,4-dihydro)-1H-pyrano[3,4-c]pyridiny, 7-(3,4-dihydro)-1H-pyrano[4,3-c]pyridiny, 7-(3,4-dihydro)-2H-pyrano[3,2-c]pyridiny, 5-(3,4-dihydro)-2H-pyrano[3,2-c]pyridiny, 5-(3,4-dihydro)-1H-pyrano[4,3-c]pyridiny, 8-(3,4-dihydro)-1H-pyrano[3,4-c]pyridiny, 8-(3,4-dihydro)-2H-pyrano[2,3-c]pyridiny, 7-(3,4-dihydro)-2H-
- 25 pyrano[2,3-b]pyridiny, 2-(5,6-dihydro)-1H-pyrano[3,4-b]pyridiny, 2-(5,6-dihydro)-2H-pyrano[4,3-b]pyridiny, 6-(3,4-dihydro)-2H-pyrano[3,2-b]pyridiny, 5-1H-pyrrolo[2,3-c]pyridiny, 6-1H-pyrrolo[3,2-c]pyridiny, 4-1H-pyrrolo[3,2-c]pyridiny, 7-1H-pyrrolo[2,3-c]pyridiny, 6-1H-pyrrolo[2,3-b]pyridiny, 5-1H-pyrrolo[3,2-b]pyridiny, 5-(2,3-dihydro)-1H-pyrrolo[2,3-c]pyridiny, 6-(2,3-dihydro)-1H-pyrrolo[3,2-c]pyridiny, 4-
- 30 (2,3-dihydro)-1H-pyrrolo[3,2-c]pyridiny, 7-(2,3-dihydro)-1H-pyrrolo[2,3-c]pyridiny, 6-(2,3-dihydro)-1H-pyrrolo[2,3-b]pyridiny, 5-(2,3-dihydro)-1H-pyrrolo[3,2-b]pyridiny, 6-(1,3-dihydro)-1H-pyrrolo[3,4-c]pyridiny, 4-(1,3-dihydro)-1H-pyrrolo[3,4-c]pyridiny, 2-(5,7-dihydro)-1H-pyrrolo[3,4-b]pyridiny, 6-1,7-naphthyridiny, 6-2,7-naphthyridiny, 7-2,6-naphthyridiny, 7-1,6-naphthyridiny, 5-1,6-naphthyridiny, 5-
- 35 2,6-naphthyridiny, 8-2,7-naphthyridiny, 8-1,7-naphthyridiny, 7-1,8-naphthyridiny, 2-1,7-naphthyridiny, 2-1,6-naphthyridiny, 6-1,5-naphthyridiny, 6-(1,2,3,4-

- tetrahydro)-1,7-naphthyridinyl, 6-(1,2,3,4-tetrahydro)-2,7-naphthyridinyl, 7-(1,2,3,4-tetrahydro)-2,6-naphthyridinyl, 7-(1,2,3,4-tetrahydro)-1,6-naphthyridinyl, 5-(1,2,3,4-tetrahydro)-1,6-naphthyridinyl, 5-(1,2,3,4-tetrahydro)-2,6-naphthyridinyl, 8-(1,2,3,4-tetrahydro)-2,7-naphthyridinyl, 8-(1,2,3,4-tetrahydro)-1,7-naphthyridinyl, 7-(1,2,3,4-tetrahydro)-1,8-naphthyridinyl, 2-(5,6,7,8-tetrahydro)-1,7-naphthyridinyl, 2-(5,6,7,8-tetrahydro)-1,6-naphthyridinyl, 6-(1,2,3,4-tetrahydro)-1,5-naphthyridinyl, 1-naphthyl, 2-naphthyl, 5-(1,2,3,4-tetrahydro)-naphthyl, 6-(1,2,3,4-tetrahydro)-naphthyl, 4-(2,3-dihydro)-1H-indenyl, 5-(2,3-dihydro)-1H-indenyl, 5-benzofuranyl, 4-benzofuranyl, 6-benzofuranyl, 7-benzofuranyl, 5-(2,3-dihydro)-benzofuranyl, 4-(2,3-dihydro)-benzofuranyl, 6-(2,3-dihydro)-benzofuranyl, 7-(2,3-dihydro)-benzofuranyl, 4-(1,3-dihydro)-isobenzofuran, 5-(1,3-dihydro)-isobenzofuran, 4-1H-indolyl, 5-1H-indolyl, 6-1H-indolyl, 7-1H-indolyl, 4-(2,3-dihydro)-1H-indolyl, 5-(2,3-dihydro)-1H-indolyl, 6-(2,3-dihydro)-1H-indolyl, 7-(2,3-dihydro)-1H-indolyl, 4-(1,3-dihydro)-1H-isoindolyl, 5-(1,3-dihydro)-1H-isoindolyl, 5-(3,4-dihydro)-1H-2-benzopyranyl, 6-(3,4-dihydro)-1H-2-benzopyranyl, 7-(3,4-dihydro)-1H-2-benzopyranyl, 8-(3,4-dihydro)-1H-2-benzopyranyl, 5-(3,4-dihydro)-2H-1-benzopyranyl, 6-(3,4-dihydro)-2H-1-benzopyranyl, 7-(3,4-dihydro)-2H-1-benzopyranyl, 8-(3,4-dihydro)-2H-1-benzopyranyl, 5-(1,2,3,4-tetrahydro)-isoquinolinyl, 6-(1,2,3,4-tetrahydro)-isoquinolinyl, 7-(1,2,3,4-tetrahydro)-isoquinolinyl, 8-(1,2,3,4-tetrahydro)-isoquinolinyl, 5-(1,2,3,4-tetrahydro)-quinolinyl, 6-(1,2,3,4-tetrahydro)-quinolinyl, 7-(1,2,3,4-tetrahydro)-quinolinyl, 8-(1,2,3,4-tetrahydro)-quinolinyl, 5-thieno[2,3-c]pyridinyl, 6-thieno[3,2-c]pyridinyl, 4-thieno[3,2-c]pyridinyl, 7-thieno[2,3-c]pyridinyl, 6-thieno[2,3-b]pyridinyl, 5-thieno[3,2-b]pyridinyl, 5-(2,3-dihydro)-thieno[2,3-c]pyridinyl, 6-(2,3-dihydro)-thieno[3,2-c]pyridinyl, 4-(2,3-dihydro)-thieno[3,2-c]pyridinyl, 7-(2,3-dihydro)-thieno[2,3-c]pyridinyl, 6-(2,3-dihydro)-thieno[2,3-b]pyridinyl, 5-(2,3-dihydro)-thieno[3,2-b]pyridinyl, 6-(1,3-dihydro)-thieno[3,4-c]pyridinyl, 4-(1,3-dihydro)-thieno[3,4-c]pyridinyl, 2-(5,7-dihydro)-thieno[3,4-b]pyridinyl, 6-(3,4-dihydro)-2H-thiopyrano[2,3-c]pyridinyl, 6-(3,4-dihydro)-1H-thiopyrano[3,4-c]pyridinyl, 7-(3,4-dihydro)-1H-thiopyrano[4,3-c]pyridinyl, 7-(3,4-dihydro)-2H-thiopyrano[3,2-c]pyridinyl, 5-(3,4-dihydro)-2H-thiopyrano[3,2-c]pyridinyl, 5-(3,4-dihydro)-1H-thiopyrano[4,3-c]pyridinyl, 8-(3,4-dihydro)-1H-thiopyrano[3,4-c]pyridinyl, 8-(3,4-dihydro)-2H-thiopyrano[2,3-c]pyridinyl, 7-(3,4-dihydro)-2H-thiopyrano[2,3-b]pyridinyl, 2-(5,6-dihydro)-1H-thiopyrano[3,4-b]pyridinyl, 2-(5,6-dihydro)-2H-thiopyrano[4,3-b]pyridinyl, 6-(3,4-dihydro)-2H-thiopyrano[3,2-b]pyridinyl, 5-benzo[b]thiophenyl, 4-benzo[b]thiophenyl, 6-benzo[b]thiophenyl, 7-benzo[b]thiophenyl, 5-(2,3-dihydro)-benzo[b]thiophenyl, 4-(2,3-dihydro)-benzo[b]thiophenyl, 6-(2,3-dihydro)-benzo[b]thiophenyl, 7-(2,3-dihydro)-

benzo[b]thiophenyl, 4-(1,3-dihydro)-benzo[c]thiophenyl, 5-(1,3-dihydro)-benzo[c]thiophenyl, 5-(3,4-dihydro)-1H-2-benzothiopyranyl, 6-(3,4-dihydro)-1H-2-benzothiopyranyl, 7-(3,4-dihydro)-1H-2-benzothiopyranyl, 8-(3,4-dihydro)-1H-2-benzothiopyranyl, 5-(3,4-dihydro)-2H-1-benzothiopyranyl, 6-(3,4-dihydro)-2H-1-benzothiopyranyl, 7-(3,4-dihydro)-2H-1-benzothiopyranyl, or 8-(3,4-dihydro)-2H-1-benzothiopyranyl; or such five or six membered ring substituted with 1, 2 or 3, C₁-C₆ alkyl, C₁-C₆ alkoxy, -OH, -CH₂OH, -(CH₂)_n-N(R₃₁)(R₃₂), -C₃-C₈ cycloalkyl, -CF₃, -halo, -CO₂(R₃₁), -CON(R₃₁)(R₃₂), -CO(R₃₁), -(CH₂)_n-N(R₃₁)(CO(R₃₃)), -(CH₂)_n-N(R₃₁)(SO₂(R₃₃)), -CN, -CH₂CF₃ or -CH(CF₃)₂, or phenyl, and the saturated ring may be optionally substituted with 1, 2 or 3, -C₁-C₆ alkyl, -C₁-C₆ alkoxy, -OH, -CH₂OH or -(CH₂)_n-N(R₃₁)(R₃₂) or one oxo (=O);

8. A compound according to Claim 7 wherein R₄ is NH₂, R₅ is -H, and R₆ is -SCH₃.

9. A compound according to Claim 8 wherein R₁ is a five or six membered saturated or unsaturated ring selected from the group consisting of 3-isoquinolinyl, 1-isoquinolinyl, 2-quinolinyl, 3-quinolinyl, 3-(5,6,7,8-tetrahydro)-isoquinolinyl, 1-(5,6,7,8-tetrahydro)-isoquinolinyl, 2-(5,6,7,8-tetrahydro)-quinolinyl, 3-(5,6,7,8-tetrahydro)-quinolinyl, 3-(5,6-dihydro)-2H-2-pyrindinyl, 1-(5,6-dihydro)-2H-2-pyrindinyl, 2-(5,6-dihydro)-1H-1-pyrindinyl, 3-(5,6-dihydro)-1H-1-pyrindinyl, 5-furo[2,3-c]pyridinyl, 6-furo[3,2-c]pyridinyl, 4-furo[3,2-c]pyridinyl, 7-furo[2,3-c]pyridinyl, 6-furo[2,3-b]pyridinyl, 5-furo[3,2-b]pyridinyl, 5-(2,3-dihydro)-furo[2,3-c]pyridinyl, 6-(2,3-dihydro)-furo[3,2-c]pyridinyl, 4-(2,3-dihydro)-furo[3,2-c]pyridinyl, 7-(2,3-dihydro)-furo[2,3-c]pyridinyl, 6-(2,3-dihydro)-furo[2,3-b]pyridinyl, 5-(2,3-dihydro)-furo[3,2-b]pyridinyl, 6-(1,3-dihydro)-furo[3,4-c]pyridinyl, 4-(1,3-dihydro)-furo[3,4-c]pyridinyl, 2-(5,7-dihydro)-furo[3,4-b]pyridinyl, 6-(3,4-dihydro)-2H-pyrano[2,3-c]pyridinyl, 6-(3,4-dihydro)-1H-pyrano[3,4-c]pyridinyl, 7-(3,4-dihydro)-1H-pyrano[4,3-c]pyridinyl, 7-(3,4-dihydro)-2H-pyrano[3,2-c]pyridinyl, 5-(3,4-dihydro)-2H-pyrano[3,2-c]pyridinyl, 5-(3,4-dihydro)-1H-pyrano[4,3-c]pyridinyl, 8-(3,4-dihydro)-1H-pyrano[3,4-c]pyridinyl, 8-(3,4-dihydro)-2H-pyrano[2,3-c]pyridinyl, 7-(3,4-dihydro)-2H-pyrano[2,3-b]pyridinyl, 2-(5,6-dihydro)-1H-pyrano[3,4-b]pyridinyl, 2-(5,6-dihydro)-2H-pyrano[4,3-b]pyridinyl and 6-(3,4-dihydro)-2H-pyrano[3,2-b]pyridinyl or such five or six membered ring substituted 1, 2 or 3, C₁-C₆ alkyl, C₁-C₆ alkoxy, -OH, -CH₂OH, -(CH₂)_n-N(R₃₁)(R₃₂), -C₃-C₈ cycloalkyl, -CF₃, -halo, -CO₂(R₃₁), -CON(R₃₁)(R₃₂), -CO(R₃₁), -(CH₂)_n-N(R₃₁)(CO(R₃₃)), -(CH₂)_n-N(R₃₁)(SO₂(R₃₃)), -CN, -CH₂CF₃ or -CH(CF₃)₂, or phenyl, and the saturated ring may be optionally substituted with 1, 2

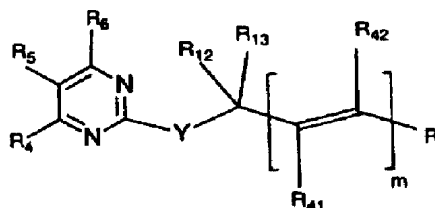
or 3, -C₁-C₆ alkyl, -C₁-C₆ alkoxy, -OH, -CH₂OH or -(CH₂)_n-N(R₃₁)(R₃₂) or one oxo (=O).

10. A compound according to Claim 1 and selected from the group consisting of:
 - 5 (E)-N,N-Diethyl-4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-2-butenamide (Cpd# 194)
 - (E)-1-[4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-1-oxo-2-butenyl]pyrrolidine (Cpd# 199)
 - (E)-N-ethyl-N-methyl-4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-2-butenamide
 - 10 (Cpd# 203)
 - (E)-N,N-Diethyl-4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-2-pentenamide (Cpd# 207)
 - 4-Amino-6-methylthio-2-(1-(3-isoquinolyl)ethyl)thio-pyrimidine (Cpd# 230)
 - 4-Amino-5-bromo-6-methylthio-2-(1-(3-isoquinolyl)ethyl)thio-pyrimidine (Cpd#
 - 15 231)
 - 4-Amino-6-methylthio-2-(1-(3-(5,6,7,8-tetrahydroisoquinolyl))ethyl)thio-pyrimidine (Cpd#233)
 - 4-Amino-6-methylthio-2-(1-(7-chlorofuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd# 237)
 - 20 4-Amino-6-methylthio-2-(1-(furo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine (Cpd# 238)
 - 4-Amino-6-methylthio-2-(1-(7-chloro-2-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd #240)
 - 4-Amino-6-methylthio-2-(1-(2-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-
 - 25 pyrimidine (Cpd #242)
 - 4-Amino-6-methylthio-2-(1-(2-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd #243)
 - 4-Amino-6-methylthio-2-(1-(3-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd #246)
 - 30 4-Amino-6-methylthio-2-(1-(2,3-dihydrofuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd #247)
 - 4-Amino-6-methylthio-2-(1-(3,3-dimethyl-2,3-dihydrofuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd #248)
 - 4-Amino-6-methylthio-2-(1-(3-ethylfuro[2,3c]pyridine-5-yl)ethyl)thio-
 - 35 pyrimidine (Cpd #249)
 - 4-Amino-6-methylthio-2-(1-(7-chloro-3,3-dimethyl-2,3-

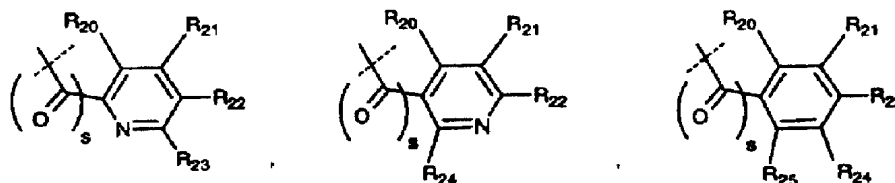
- dihydrofuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd #250)
 4-Amino-6-methylthio-2-(1-(7-chloro-3-ethylfuro-[2,3c]pyridine-5-yl)ethyl)thio-
 pyrimidine (Cpd #251)
 4-Amino-6-methylthio-2-(1-(3-(1-methylethyl)furo[2,3c]-pyridin-5-yl)ethyl)thio-
 5 pyrimidine (Cpd #252)
 4-Amino-6-methylthio-2-(1-(3-chlorofuro[2,3c]pyridine-5-yl)ethyl)thio-
 pyrimidine. (Cpd #282)
 4-Amino-6-methylthio-2-(1-(3,7-dichlorofuro[2,3c]pyridine-5-yl)ethyl)thio-
 pyrimidine, (Cpd #283)
 10 4-Amino-6-methylthio-2-(1-(3-bromofuro[2,3c]pyridine-5-yl)ethyl)thio-
 pyrimidine, (Cpd #284)
 4-Amino-6-methylthio-2-(1-(3-bromo-7-chlorofuro[2,3c]pyridine-5-yl)ethyl)thio-
 pyrimidine, (Cpd #285)
 4-Amino-6-methylthio-2-(1-(7-chloro-3-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-
 15 pyrimidine, (Cpd #286)
 4-Amino-6-trifluoromethyl-2-(1-(7-chloro-3,3-dimethyl-2,3-
 dihydrofuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine, (Cpd #287)
 (R)-(+)-4-Amino-6-methylthio-2-(1-(3-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-
 pyrimidine (Cd #289)
 20 (S)-(-)-4-Amino-6-methylthio-2-(1-(3-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-
 pyrimidine Cpd #290
 (S)-(-)-4-Amino-6-trifluoromethyl-2-(1-(3-methylfuro[2,3c]pyridin-5-
 yl)ethylthio)-pyrimidine (Cpd #297)
 (S)-(-)-4-Amino-6-methylthio-2-(1-(furo[2,3c]pyridin-5-yl)ethylthio)-pyrimidine
 25 (Cpd #1);
 and pharmaceutically acceptable salts, hydrates, N-oxides and solvates thereof.

11. A method of treating an individual infected with the human
 immunodeficiency virus (HIV) which comprises administering an effective amount of
 30 an anti-AIDS compound of Formula I

5

10 where m is 0 or 1;
 R^1 is selected from the group consisting of $-C\equiv CH$, $-CO_2R_{53}$, $-CONR_{54}R_{55}$,

15



20

where s is 0 or 1 and R_{20} , R_{21} , R_{22} , R_{23} , R_{24} , and R_{25} are the same or different and are selected from $-H$, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkoxy, C_1-C_6 alkylthio, $-C_3-C_8$ cycloalkyl, $-CF_3$, $-NO_2$, $-halo$, $-OH$, $-CN$, phenyl, phenylthio, $-styryl$, $-CO_2(R_{31})$, $-CON(R_{31})(R_{32})$, $-CO(R_{31})$, $-(CH_2)_n-N(R_{31})(R_{32})$, $-C(OH)(R_{31})(R_{33})$, $-(CH_2)_n-N(R_{31})(CO(R_{33}))$, $(CH_2)_n-N(R_{31})(SO_2(R_{33}))$, or where R_{20} and R_{21} , or R_{21} and R_{22} , or

25

R_{22} and R_{23} are taken together to form a five or six-membered saturated or unsaturated ring containing 0 or 1 oxygen, nitrogen or sulfur, where the unsaturated ring may be optionally substituted with 1, 2 or 3, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-OH$, $-CH_2OH$, $-(CH_2)_n-N(R_{31})(R_{32})$, $-C_3-C_8$ cycloalkyl, $-CF_3$, $-halo$, $-CO_2(R_{31})$, $-CON(R_{31})(R_{32})$, $-CO(R_{31})$, $-(CH_2)_n-N(R_{31})(CO(R_{33}))$, $-(CH_2)_n-N(R_{31})(SO_2(R_{33}))$, $-CN$, CH_2CF_3 or $-CH(CF_3)_2$, or phenyl, and the saturated ring may be optionally substituted with 1, 2 or 3, $-C_1-C_6$ alkyl, $-C_1-C_6$ alkoxy, $-OH$, $-CH_2OH$ or $-(CH_2)_n-N(R_{31})(R_{32})$ or one oxo ($=O$);

30

where n is 0-3 and R_{31} , R_{32} , and R_{33} are the same or different and are selected from

35

-H,

C₁-C₆ alkyl,

phenyl optionally substituted with 1, 2, or 3 -halo, C₁-C₆ alkyl,

C₁-C₆ alkoxy, -CF₃, -OH or -CN,

5 or where R₃₁ and R₃₂ taken together with the attached nitrogen to form a ring selected from -pyrrolidinyl, -piperidinyl, -4-morpholinyl, -4-thiomorpholinyl, -4-piperazinyl, -4-(1-C₁-C₆alkyl)piperazinyl,

or a member selected from the group consisting of:

1-cyclohexenyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 2-imidazolyl,
 10 4-imidazolyl, 2-benzothiazolyl, 2-benzoxazolyl, 2-benzimidazolyl, 2-oxazolyl,
 4-oxazolyl, 2-thiazolyl, 3-isoxazolyl, 5-isoxazolyl, 5-methyl-3-isoxazolyl, 5-phenyl-3-isoxazolyl, 4-thiazolyl, 3-methyl-2-pyrazinyl, 5-methyl-2-pyrazinyl, 6-methyl-2-pyrazinyl, 5-chloro-2-thienyl, 3-furyl, benzofuran-2-yl, benzothien-2-yl, 2H-1-benzopyran-3-yl, 2,3-dihydrobenzopyran-5-yl, 1-methylimidazol-2-yl,
 15 quinoxalin-2-yl, piperon-5-yl, 4,7-dichlorobenzoxazol-2-yl, 4,6-dimethylpyrimidin-2-yl, 4-methylpyrimidin-2-yl, 2,4-dimethylpyrimidin-6-yl, 2-methylpyrimidin-4-yl, 4-methylpyrimidin-6-yl, 6-chloropiperon-5-yl, 5-chloroimidazo[1,2-a]pyridin-2-yl, 1-H-inden-3-yl, 1-H-2-methyl-inden-2-yl, 3,4-dihydronaphth-1-yl, S-4-isopropenylcyclohexen-1-yl or 4-dihydronaphth-2-yl;

20 where R₅₃ is selected from the group consisting of -H, C₁-C₆alkyl, C₃-C₆cycloalkyl, phenyl (optionally substituted with 1, 2, or 3 -halo, C₁-C₆ alkyl, C₁-C₆ alkoxy, -CF₃, -OH, -CN), or a five or six-membered unsaturated ring containing 0 or 1 oxygen, nitrogen or sulfur, where the unsaturated ring may be optionally substituted with -H, C₁-C₆ alkyl,

25 C₁-C₆ alkoxy, -OH, -CH₂OH, or -(CH₂)_n-N(R₃₁)(R₃₂);

where R₅₄ and R₅₅ being the same or different are selected from -H, C₁-C₆ alkyl, allyl, or phenyl (optionally substituted with 1, 2, or 3 -halo, C₁-C₆ alkyl, C₁-C₆ alkoxy or -CF₃), or taken together with the attached nitrogen to form a ring selected from -pyrrolidinyl, -piperidinyl, -4-morpholinyl, -4-thiomorpholinyl, -4-piperazinyl, -
 30 4-(1-C₁-C₆alkyl)piperazinyl;

R₄₁ and R₄₂, being the same or different, are selected from the group consisting of -H and C₁-C₄ alkyl;

R₁₂ is selected from the group consisting of -H, C₁-C₆ alkyl, -C₃-C₆ cycloalkyl, -CN, -C(O)NH₂, -C(O)N(C₁-C₆alkyl)(C₁-C₆alkyl), -CO₂H, -CO₂(C₁-C₆alkyl), -CH₂OH, -CH₂NH₂ or -CF₃;
 35

R₁₃ is selected from the group consisting of -H, C₁-C₆ alkyl or -CF₃;

Y is selected from -S-, -S(O)-, -S(O)₂, or -O-;

R₄ is selected from the group consisting of -H, -OH, halo or -NR₁₅R₁₆ where R₁₅ is -H and R₁₆ is -H, C₁-C₆ alkyl, -NH₂ or R₁₅ and R₁₆ taken together with the -N form 1-pyrrolidino, 4-morpholino or 1-piperidino;

5 R₅ is selected from the group consisting of -H, -C₂H₄OH, -C₂H₄-O-TBDMS, halo,

-C₃-C₆ cycloalkyl, C₁-C₄ alkyl or C₁-C₃ alkoxy;

or R₄ and R₅ are taken together to form a five or six-membered saturated or unsaturated ring which together with the pyrimidine ring form the group consisting
10 of 7H-pyrrolo[2,3-d]pyrimidine, 5,6-dihydro-7H-pyrrolo[2,3-d]pyrimidine, furo[2,3-d]pyrimidine, 5,6-dihydro-furo[2,3-d]pyrimidine, thieno[2,3-d]pyrimidine, 5,6-dihydro-thieno[2,3-d]pyrimidine, 1H-pyrazolo[3,4-d]pyrimidine, 1H-purine, pyrimido[4,5-d]pyrimidine, pteridine, pyrido[2,3-d]pyrimidine, or quinazoline, where the unsaturated ring may be optionally substituted with 1, 2 or 3, C₁-C₆ alkyl, C₁-C₆
15 alkoxy, -OH, -CH₂OH, or

-(CH₂)_n-N(R₃₁)(R₃₂), -C₃-C₈ cycloalkyl, -CF₃, -halo, -CO₂(R₃₁), -CON(R₃₁)(R₃₂), -CO(R₃₁), -(CH₂)_n-N(R₃₁)(CO(R₃₃)), -(CH₂)_n-N(R₃₁)(SO₂(R₃₃)), and the saturated ring may be optionally substituted with 1, 2 or 3, -C₁-C₆ alkyl, -C₁-C₆ alkoxy, -OH, -CH₂OH, or -(CH₂)_n-N(R₃₁)(R₃₂) or one oxo (=O); and

20 R₆ is -S-C₁-C₆ alkyl;

and pharmaceutically acceptable salts, hydrates, N-oxides and solvates thereof;

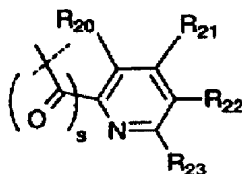
12. A method according to Claim 11 where m is 0, s is 0 and Y -S.

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13. A method according to Claim 12 where R₁₂ is CH₃ and R₁₃ is -H.

14. A method according to Claim 13 where R₄ is NH₂, R₅ is -H, and R₆ is -SCH₃.

30 15. A method according to Claim 12 where R₁ is



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16. A method according to Claim 15 wherein R_4 is NH_2 , R_5 is $-H$, and R_6 is $-SCH_3$.
17. A method according to Claim 14 wherein R_1 is a five or six membered
- 5 saturated or unsaturated ring selected from the group consisting of 3-isoquinoliny, 1-isoquinoliny, 2-quinoliny, 3-quinoliny, 3-(5,6,7,8-tetrahydro)-isoquinoliny, 1-(5,6,7,8-tetrahydro)-isoquinoliny, 2-(5,6,7,8-tetrahydro)-quinoliny, 3-(5,6,7,8-tetrahydro)-quinoliny, 3-(5,6-dihydro)-2H-2-pyrindiny, 1-(5,6-dihydro)-2H-2-pyrindiny, 2-(5,6-dihydro)-1H-1-pyrindiny, 3-(5,6-dihydro)-1H-1-pyrindiny, 5-
- 10 furo[2,3-c]pyridiny, 6-furo[3,2-c]pyridiny, 4-furo[3,2-c]pyridiny, 7-furo[2,3-c]pyridiny, 6-furo[2,3-b]pyridiny, 5-furo[3,2-b]pyridiny, 5-(2,3-dihydro)-furo[2,3-c]pyridiny, 6-(2,3-dihydro)-furo[3,2-c]pyridiny, 4-(2,3-dihydro)-furo[3,2-c]pyridiny, 7-(2,3-dihydro)-furo[2,3-c]pyridiny, 6-(2,3-dihydro)-furo[2,3-b]pyridiny, 5-(2,3-dihydro)-furo[3,2-b]pyridiny, 6-(1,3-dihydro)-furo[3,4-c]pyridiny, 4-(1,3-dihydro)-
- 15 furo[3,4-c]pyridiny, 2-(5,7-dihydro)-furo[3,4-b]pyridiny, 6-(3,4-dihydro)-2H-pyrano[2,3-c]pyridiny, 6-(3,4-dihydro)-1H-pyrano[3,4-c]pyridiny, 7-(3,4-dihydro)-1H-pyrano[4,3-c]pyridiny, 7-(3,4-dihydro)-2H-pyrano[3,2-c]pyridiny, 5-(3,4-dihydro)-2H-pyrano[3,2-c]pyridiny, 5-(3,4-dihydro)-1H-pyrano[4,3-c]pyridiny, 8-(3,4-dihydro)-1H-pyrano[3,4-c]pyridiny, 8-(3,4-dihydro)-2H-pyrano[2,3-c]pyridiny, 7-(3,4-dihydro)-2H-
- 20 pyrano[2,3-b]pyridiny, 2-(5,6-dihydro)-1H-pyrano[3,4-b]pyridiny, 2-(5,6-dihydro)-2H-pyrano[4,3-b]pyridiny, 6-(3,4-dihydro)-2H-pyrano[3,2-b]pyridiny, 5-1H-pyrrolo[2,3-c]pyridiny, 6-1H-pyrrolo[3,2-c]pyridiny, 4-1H-pyrrolo[3,2-c]pyridiny, 7-1H-pyrrolo[2,3-c]pyridiny, 6-1H-pyrrolo[2,3-b]pyridiny, 5-1H-pyrrolo[3,2-b]pyridiny, 5-(2,3-dihydro)-1H-pyrrolo[2,3-c]pyridiny, 6-(2,3-dihydro)-1H-pyrrolo[3,2-c]pyridiny, 4-
- 25 (2,3-dihydro)-1H-pyrrolo[3,2-c]pyridiny, 7-(2,3-dihydro)-1H-pyrrolo[2,3-c]pyridiny, 6-(2,3-dihydro)-1H-pyrrolo[2,3-b]pyridiny, 5-(2,3-dihydro)-1H-pyrrolo[3,2-b]pyridiny, 6-(1,3-dihydro)-1H-pyrrolo[3,4-c]pyridiny, 4-(1,3-dihydro)-1H-pyrrolo[3,4-c]pyridiny, 2-(5,7-dihydro)-1H-pyrrolo[3,4-b]pyridiny, 6-1,7-naphthyridiny, 6-2,7-naphthyridiny, 7-2,6-naphthyridiny, 7-1,6-naphthyridiny, 5-1,6-naphthyridiny, 5-
- 30 2,6-naphthyridiny, 8-2,7-naphthyridiny, 8-1,7-naphthyridiny, 7-1,8-naphthyridiny, 2-1,7-naphthyridiny, 2-1,6-naphthyridiny, 6-1,5-naphthyridiny, 6-(1,2,3,4-tetrahydro)-1,7-naphthyridiny, 6-(1,2,3,4-tetrahydro)-2,7-naphthyridiny, 7-(1,2,3,4-tetrahydro)-2,6-naphthyridiny, 7-(1,2,3,4-tetrahydro)-1,6-naphthyridiny, 5-(1,2,3,4-tetrahydro)-1,6-naphthyridiny, 5-(1,2,3,4-tetrahydro)-2,6-naphthyridiny, 8-(1,2,3,4-tetrahydro)-2,7-naphthyridiny, 8-(1,2,3,4-tetrahydro)-1,7-naphthyridiny, 7-(1,2,3,4-tetrahydro)-1,8-naphthyridiny, 2-(5,6,7,8-tetrahydro)-1,7-naphthyridiny, 2-(5,6,7,8-
- 35 tetrahydro)-1,8-naphthyridiny, 2-(5,6,7,8-tetrahydro)-1,7-naphthyridiny, 2-(5,6,7,8-

- tetrahydro)-1,6-naphthyridinyl, 6-(1,2,3,4-tetrahydro)-1,5-naphthyridinyl, 1-naphthyl, 2-naphthyl, 5-(1,2,3,4-tetrahydro)-naphthyl, 6-(1,2,3,4-tetrahydro)-naphthyl, 4-(2,3-dihydro)-1H-indenyl, 5-(2,3-dihydro)-1H-indenyl, 5-benzofuranyl, 4-benzofuranyl, 6-benzofuranyl, 7-benzofuranyl, 5-(2,3-dihydro)-benzofuranyl, 4-(2,3-dihydro)-
- 5 benzofuranyl, 6-(2,3-dihydro)-benzofuranyl, 7-(2,3-dihydro)-benzofuranyl, 4-(1,3-dihydro)-isobenzofuran, 5-(1,3-dihydro)-isobenzofuran, 4-1H-indolyl, 5-1H-indolyl, 6-1H-indolyl, 7-1H-indolyl, 4-(2,3-dihydro)-1H-indolyl, 5-(2,3-dihydro)-1H-indolyl, 6-(2,3-dihydro)-1H-indolyl, 7-(2,3-dihydro)-1H-indolyl, 4-(1,3-dihydro)-1H-isoindolyl, 5-(1,3-dihydro)-1H-isoindolyl, 5-(3,4-dihydro)-1H-2-benzopyranyl, 6-(3,4-dihydro)-1H-2-
- 10 benzopyranyl, 7-(3,4-dihydro)-1H-2-benzopyranyl, 8-(3,4-dihydro)-1H-2-benzopyranyl, 5-(3,4-dihydro)-2H-1-benzopyranyl, 6-(3,4-dihydro)-2H-1-benzopyranyl, 7-(3,4-dihydro)-2H-1-benzopyranyl, 8-(3,4-dihydro)-2H-1-benzopyranyl, 5-(1,2,3,4-tetrahydro)-isoquinolinyl, 6-(1,2,3,4-tetrahydro)-isoquinolinyl, 7-(1,2,3,4-tetrahydro)-isoquinolinyl, 8-(1,2,3,4-tetrahydro)-isoquinolinyl, 5-(1,2,3,4-tetrahydro)-quinolinyl, 6-
- 15 (1,2,3,4-tetrahydro)-quinolinyl, 7-(1,2,3,4-tetrahydro)-quinolinyl, 8-(1,2,3,4-tetrahydro)-quinolinyl, 5-thieno[2,3-c]pyridinyl, 6-thieno[3,2-c]pyridinyl, 4-thieno[3,2-c]pyridinyl, 7-thieno[2,3-c]pyridinyl, 6-thieno[2,3-b]pyridinyl, 5-thieno[3,2-b]pyridinyl, 5-(2,3-dihydro)-thieno[2,3-c]pyridinyl, 6-(2,3-dihydro)-thieno[3,2-c]pyridinyl, 4-(2,3-dihydro)-thieno[3,2-c]pyridinyl, 7-(2,3-dihydro)-thieno[2,3-
- 20 c]pyridinyl, 6-(2,3-dihydro)-thieno[2,3-b]pyridinyl, 5-(2,3-dihydro)-thieno[3,2-b]pyridinyl, 6-(1,3-dihydro)-thieno[3,4-c]pyridinyl, 4-(1,3-dihydro)-thieno[3,4-c]pyridinyl, 2-(5,7-dihydro)-thieno[3,4-b]pyridinyl 6-(3,4-dihydro)-2H-thiopyrano[2,3-c]pyridinyl, 6-(3,4-dihydro)-1H-thiopyrano[3,4-c]pyridinyl, 7-(3,4-dihydro)-1H-thiopyrano[4,3-c]pyridinyl, 7-(3,4-dihydro)-2H-thiopyrano[3,2-c]pyridinyl,
- 25 5-(3,4-dihydro)-2H-thiopyrano[3,2-c]pyridinyl, 5-(3,4-dihydro)-1H-thiopyrano[4,3-c]pyridinyl, 8-(3,4-dihydro)-1H-thiopyrano[3,4-c]pyridinyl, 8-(3,4-dihydro)-2H-thiopyrano[2,3-c]pyridinyl, 7-(3,4-dihydro)-2H-thiopyrano[2,3-b]pyridinyl, 2-(5,6-dihydro)-1H-thiopyrano[3,4-b]pyridinyl, 2-(5,6-dihydro)-2H-thiopyrano[4,3-b]pyridinyl, 6-(3,4-dihydro)-2H-thiopyrano[3,2-b]pyridinyl, 5-benzo[b]thiophenyl, 4-
- 30 benzo[b]thiophenyl, 6-benzo[b]thiophenyl, 7-benzo[b]thiophenyl, 5-(2,3-dihydro)-benzo[b]thiophenyl, 4-(2,3-dihydro)-benzo[b]thiophenyl, 6-(2,3-dihydro)-benzo[b]thiophenyl, 7-(2,3-dihydro)-benzo[b]thiophenyl, 4-(1,3-dihydro)-benzo[c]thiophenyl, 5-(1,3-dihydro)-benzo[c]thiophenyl, 5-(3,4-dihydro)-1H-2-benzothiopyranyl, 6-(3,4-dihydro)-1H-2-benzothiopyranyl, 7-(3,4-dihydro)-1H-2-
- 35 benzothiopyranyl, 8-(3,4-dihydro)-1H-2-benzothiopyranyl, 5-(3,4-dihydro)-2H-1-benzothiopyranyl, 6-(3,4-dihydro)-2H-1-benzothiopyranyl, 7-(3,4-dihydro)-2H-1-

benzothiopyranyl or 8-(3,4-dihydro)-2H-1-benzothiopyranyl; or such five or six membered ring substituted with 1, 2 or 3, C₁-C₆ alkyl, C₁-C₆ alkoxy, -OH, -CH₂OH, -(CH₂)_n-N(R₃₁)(R₃₂), -C₃-C₈ cycloalkyl, -CF₃, -halo, -CO₂(R₃₁), -CON(R₃₁)(R₃₂), -CO(R₃₁), -(CH₂)_n-N(R₃₁)(CO(R₃₃)), -(CH₂)_n-N(R₃₁)(SO₂(R₃₃)), -CN, -CH₂CF₃ or -CH(CF₃)₂, or phenyl, and the saturated ring may be optionally substituted with 1, 2 or 3, -C₁-C₆ alkyl, -C₁-C₆ alkoxy, -OH, -CH₂OH or -(CH₂)_n-N(R₃₁)(R₃₂) or one oxo (=O).

18. A method according to Claim 17 wherein R₄ is NH₂, R₅ is -H, and R₆ is -SCH₃.

10

19. A method according to Claim 18 wherein R₁ is a five or six membered saturated or unsaturated ring selected from the group consisting of 3-isoquinoliny, 1-isoquinoliny, 2-quinoliny, 3-quinoliny, 3-(5,6,7,8-tetrahydro)-isoquinoliny, 1-(5,6,7,8-tetrahydro)-isoquinoliny, 2-(5,6,7,8-tetrahydro)-quinoliny, 3-(5,6,7,8-tetrahydro)-quinoliny, 3-(5,6-dihydro)-2H-2-pyrindiny, 1-(5,6-dihydro)-2H-2-pyrindiny, 2-(5,6-dihydro)-1H-1-pyrindiny, 3-(5,6-dihydro)-1H-1-pyrindiny, 5-furo[2,3-c]pyridiny, 6-furo[3,2-c]pyridiny, 4-furo[3,2-c]pyridiny, 7-furo[2,3-c]pyridiny, 6-furo[2,3-b]pyridiny, 5-furo[3,2-b]pyridiny, 5-(2,3-dihydro)-furo[2,3-c]pyridiny, 6-(2,3-dihydro)-furo[3,2-c]pyridiny, 4-(2,3-dihydro)-furo[3,2-c]pyridiny, 7-(2,3-dihydro)-furo[2,3-c]pyridiny, 6-(2,3-dihydro)-furo[2,3-b]pyridiny, 5-(2,3-dihydro)-furo[3,2-b]pyridiny, 6-(1,3-dihydro)-furo[3,4-c]pyridiny, 4-(1,3-dihydro)-furo[3,4-c]pyridiny, 2-(5,7-dihydro)-furo[3,4-b]pyridiny, 6-(3,4-dihydro)-2H-pyrano[2,3-c]pyridiny, 6-(3,4-dihydro)-1H-pyrano[3,4-c]pyridiny, 7-(3,4-dihydro)-1H-pyrano[4,3-c]pyridiny, 7-(3,4-dihydro)-2H-pyrano[3,2-c]pyridiny, 5-(3,4-dihydro)-2H-pyrano[3,2-c]pyridiny, 5-(3,4-dihydro)-1H-pyrano[4,3-c]pyridiny, 8-(3,4-dihydro)-1H-pyrano[3,4-c]pyridiny, 8-(3,4-dihydro)-2H-pyrano[2,3-c]pyridiny, 7-(3,4-dihydro)-2H-pyrano[2,3-b]pyridiny, 2-(5,6-dihydro)-1H-pyrano[3,4-b]pyridiny, 2-(5,6-dihydro)-2H-pyrano[4,3-b]pyridiny and 6-(3,4-dihydro)-2H-pyrano[3,2-b]pyridiny or such five or six membered ring with 1, 2 or 3, C₁-C₆ alkyl, C₁-C₆ alkoxy, -OH, -CH₂OH, -(CH₂)_n-N(R₃₁)(R₃₂), -C₃-C₈ cycloalkyl, -CF₃, -halo, -CO₂(R₃₁), -CON(R₃₁)(R₃₂), -CO(R₃₁), -(CH₂)_n-N(R₃₁)(CO(R₃₃)), -(CH₂)_n-N(R₃₁)(SO₂(R₃₃)), -CN, -CH₂CF₃ or -CH(CF₃)₂, or phenyl, and the saturated ring may be optionally substituted with 1, 2 or 3, -C₁-C₆ alkyl, -C₁-C₆ alkoxy, -OH, -CH₂OH or -(CH₂)_n-N(R₃₁)(R₃₂) or one oxo (=O).

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20. A method of treating an individual infected with the human immunodeficiency virus (HIV) according to Claim 11 where the (1) infected individual is asymptomatic but tests positive for the HIV antigen, (2) infected individual is symptomatically sick but does not have "full blown AIDS", (3) individual infected
 5 with the human immunodeficiency virus (HIV) has "full blown AIDS".

21. A method of treating an individual infected with the human immunodeficiency virus (HIV) according to claim 11 where the administration is oral and the effective dose is from about 0.10 mg/kg/day to about 500 mg/kg/day.

10

22. A method of treating an individual infected with the human immunodeficiency virus (HIV) according to claim 11 where the compound is selected from the group consisting of

(*E*)-*N,N*-Diethyl-4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-2-butenamide

15 (Cpd# 194)

(*E*)-1-[4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-1-oxo-2-butenyl]pyrrolidine

(Cpd# 199)

(*E*)-*N*-ethyl-*N*-methyl-4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-2-butenamide

(Cpd# 203)

20 (*E*)-*N,N*-Diethyl-4-[(4-amino-6-methylthio-2-pyrimidinyl)thio]-2-pentenamide

(Cpd# 207)

4-Amino-6-methylthio-2-(1-(3-isoquinolyl)ethyl)thio-pyrimidine (Cpd# 230)

4-Amino-5-bromo-6-methylthio-2-(1-(3-isoquinolyl)ethyl)thio-pyrimidine (Cpd#

231)

25 4-Amino-6-methylthio-2-(1-(3-(5,6,7,8-tetrahydroisoquinolyl))ethyl)thio-pyrimidine (Cpd#233)

4-Amino-6-trifluoromethyl-2-(1-(3-(5,6,7,8-tetrahydro-isoquinolyl))ethyl)thio-pyrimidine (Cpd# 234)

4-Amino-6-methylthio-2-(1-(7-chlorofuro[2,3c]pyridine-5-yl)ethyl)thio-

30 pyrimidine (Cpd# 237)

4-Amino-6-methylthio-2-(1-(furo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine (Cpd#

238)

4-Amino-6-trifluoromethyl-2-(1-(furo[2,3-c]pyridin-5-yl)ethyl)thio-pyrimidine

(Cpd# 239)

35 4-Amino-6-methylthio-2-(1-(7-chloro-2-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd # 240)

- 4-Amino-6-trifluoromethyl-2-(1-(7-chloro-2-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd# 241)
- 4-Amino-6-methylthio-2-(1-(2-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd #242)
- 5 4-Amino-6-trifluoromethyl-2-(1-(2-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd #243)
- 4-Amino-6-methylthio-2-(1-(3-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd #246)
- 4-Amino-6-methylthio-2-(1-(2,3-dihydrofuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd #247)
- 10 4-Amino-6-methylthio-2-(1-(3,3-dimethyl-2,3-dihydrofuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd# 248)
- 4-Amino-6-methylthio-2-(1-(3-ethylfuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd# 249)
- 15 4-Amino-6-methylthio-2-(1-(7-chloro-3,3-dimethyl-2,3-dihydrofuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd #250)
- 4-Amino-6-methylthio-2-(1-(7-chloro-3-ethylfuro-[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd #251)
- 4-Amino-6-methylthio-2-(1-(3-(1-methylethyl)furo[2,3c]-pyridin-5-yl)ethyl)thio-pyrimidine (Cpd #252)
- 20 4-amino-6-chloro-2-(1-(4-(1-methylpropyl)-2-pyridyl)-ethyl)thio-pyrimidine (Cpd #256)
- 4-amino-6-trifluoromethyl-2-(1-(4-(1-dimethylethyl)-2-pyridyl)-ethyl)thio-pyrimidine (Cpd #269)
- 25 4-amino-6-trifluoromethyl-2-(2-naphthylmethyl)thio-pyrimidine (Cpd #270)
- 4-amino-6-trifluoromethyl-2-((4-(1-methylethyl)-2-pyridyl)methyl)thio-pyrimidine (Cpd #271)
- 4-amino-6-trifluoromethyl-2-(1-(4-(1-methylethyl)-2-pyridyl)ethyl)thio-pyrimidine (Cpd #272)
- 30 4-amino-6-trifluoromethyl-2-((4-(1,1-dimethylethyl)-2-pyridyl)methyl)thio-pyrimidine (Cpd #273)
- 6-amino-2-(2-naphthylmethyl)thio-4-pyrimidine carbonitrile (Cpd 277),
- 4-Amino-6-methylthio-2-(1-(3-chlorofuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine. (Cpd #282)
- 35 4-Amino-6-methylthio-2-(1-(3,7-dichlorofuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine, (Cpd #283)

- 4-Amino-6-methylthio-2-(1-(3-bromofuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine, (Cpd #284)
- 4-Amino-6-methylthio-2-(1-(3-bromo-7-chlorofuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine, (Cpd #285)
- 5 4-Amino-6-methylthio-2-(1-(7-chloro-3-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine, (Cpd #286)
- 4-Amino-6-trifluoromethyl-2-(1-(7-chloro-3,3-dimethyl-2,3-dihydrofuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine, (Cpd #287) ???
- (R)-(+)-4-Amino-6-methylthio-2-(1-(3-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine (Cpd #289)
- 10 (S)-(-)-4-Amino-6-methylthio-2-(1-(3-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine
Cpd (#290)
- (S)-(-)-4-Amino-6-trifluoromethyl-2-(1-(3-methylfuro[2,3c]pyridin-5-yl)ethylthio)-pyrimidine (Cpd #297)
- 15 (S)-(-)-4-Amino-6-methylthio-2-(1-(furo[2,3c]pyridin-5-yl)ethylthio)-pyrimidine (Cpd #1);
and pharmaceutically acceptable salts, hydrates and solvates thereof.
- 20 22. A method according to Claim 21 where the compound is selected from the group consisting of (S)-(-)-4-Amino-6-methylthio-2-(1-(3-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine;
(S)-(-)-4-Amino-6-methylthio-2-(1-(3-methylfuro[2,3c]pyridin-5-yl)ethylthio)-pyrimidine esylate salt;
- 25 (S)-(-)-4-Amino-2-(3-methyl-furano[2,3c]pyridin-5-yl)ethylthio-6-trifluoromethyl-pyrimidine mesylate salt;
(S)-(-)-4-Amino-6-methylthio-2-(1-(furo[2,3c]pyridin-5-yl)ethylthio)-pyrimidine
and
(S)-(-)-4-Amino-6-methylthio-2-(1-(furo[2,3c]pyridin-5-yl)ethylthio)-pyrimidine
30 mesylate salt.
23. A compound according to Claim 1 and selected from the group consisting of
(S)-(-)-4-Amino-6-methylthio-2-(1-(3-methylfuro[2,3c]pyridine-5-yl)ethyl)thio-pyrimidine;
- 35 (S)-(-)-4-Amino-6-methylthio-2-(1-(3-methylfuro[2,3c]pyridin-5-yl)ethylthio)-pyrimidine esylate salt;

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(S)-(-)-4-Amino-6-methylthio-2-(1-(furo[2,3c]pyridin-5-yl)ethylthio)-pyrimidine
and
(S)-(-)-4-Amino-6-methylthio-2-(1-(furo[2,3c]pyridin-5-yl)ethylthio)-pyrimidine
mesylate salt.

5